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ELI H. RUBIN, *Consulting Editor*

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SYMPOSIUM ON THE TREATMENT OF LONG-TERM ILLNESS

FOREWORD

At the turn of the present century, physicians were largely occupied with finding ways and means of making childbirth safe and with prolonging the lives of those born. In the past fifty years, the advances made in the prevention of childhood diseases, in the treatment of bacterial infections of adulthood and in the management of surgical conditions of all age groups have been so rapid and substantial that today we are confronted with the Herculean task of caring for increasing numbers of elderly folk who reach seventy years and more.

The problems of dealing with an aging population are complicated and many. They are concerned not only with purely scientific efforts to fathom the complexities of cellular metabolism but with the almost equally difficult task of trying to solve the plight of those who suffer long term illness. The latter, however, is not confined to the aged, a considerable number of those afflicted are young individuals, including children. Where such patients are to be treated and who will pay for the upkeep are often more pressing problems than is the treatment of the illness itself. Yet there is ample evidence that if proper facilities were available, health and economic security could be restored for many who otherwise would be a burden on their families and the community until the final scene.

In the following pages we draw attention to a few aspects of the problem, from the social as well as the medical viewpoint. There is no doubt that in the years to come the treatment of long term illness will occupy an ever increasing amount of time and effort on the part of

physicians and agencies concerned with the health and welfare of the population

I am deeply indebted to the participants of this symposium who graciously contributed of their knowledge and skill

ELI H RUBIN, M D ,
Consulting Editor

MEDICINE IN AN AGING POPULATION

EDWARD J STIEGLITZ, M D , F.A C P *

IN common with every living organism or dynamic force, as medical science and practice grow and mature, they change Change is continuous, though asymmetric While improvement in clinical techniques may be sharply accelerated by rapid advances in scientific knowledge, other areas of practice may be developing so slowly that progress is almost imperceptible Change may involve many different facets of practice, such as the basic concepts of physiology and/or immunity, surgical, medical or psychiatric therapeutic techniques, diagnostic methods, or modes of application of medical services Change may be induced by new scientific discoveries, new application of long existing knowledge, revision and amplification of basic concepts, changing sociologic conditions, such as war, or the nearly equally disastrous though less obvious consequences of excessive socialistic paternalism,[1] the advent of epidemics, or more gradual changes in the character of diseases or of the population

It is with the effects of the last two elements mentioned that we are concerned at the moment how an aging population and a growing importance of chronic disease will alter medical practice in the future Some of the consequences of these related factors are fairly obvious Other impending changes, of perhaps even greater significance because basic and fundamental, are much less conspicuous and therefore worthy of special emphasis It is important that the medical profession exercise foresight and take aggressive leadership[2]

The history of man, both as a species and as individuals, repeatedly demonstrates that skills are developed long before judgment is adequate to guide their application The child learns how to strike matches before he acquires judgment as to when and where to do so, technology and the physical sciences have given mankind weapons of appalling destructiveness prior to the appearance of judgment sufficient to determine when not to use them So has it been with medicine, we can not escape from at least partial responsibility for the incalculably serious problem of chronic or long term illness[3] By modern techniques, applied in the prevention and cure of the acute, exogenous , infective diseases of childhood and youth, medical science and practice have enhanced longevity enormously, and

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permitted the survival of many with long-term chronic illness, protracted disability, misery and uselessness The burden of chronic disease is both individually and collectively far greater than the social consequences of high mortality from acute illnesses A man quickly dead is a lesser tragedy to himself, his family and the community than one disabled for many years

Though average longevity has increased dramatically over the last fifty years, this advance is tainted by the immense toll of prolonged disability of varying degrees The time is not yet when we, as a profession, may rest upon our laurels Life is multidimensional It must have depth and breadth as well as mere length Prolongation of life in the relatively unfit may someday jeopardize the survival of the fit The problem of chronic illness is urgent

The other papers of this symposium will deal with technics of therapy and specific chronic disease entities Thus it is appropriate to first concern ourselves with *objectives* and *principles* of medical practice in an aging and chronically ill population For example, the vitally significant objective of *prevention* of long-term illness is omitted from these collected papers The future of medical practice, at least as we envisage progress, will invoke an ever-growing concern with prevention, with health maintenance, and constructive medicine [4] The treatment of chronic disease after disablement has occurred is equivalent to locking the stable door after the horse is stolen True, such may prevent the theft of other items from the barn, but how much better to have anticipated and averted the loss [15]

Exhaustingly detailed statistics[6] are not needed to indicate the magnitude of the medical problems raised by the recent dramatic increase in average longevity In 1850, the average life expectancy at birth was approximately 40 years in the New England States At the turn of the century, the average for the United States as a whole was 47 years, by 1930 it had jumped to 60 years, in 1940 it increased to 63 years for white members of the American population Infants born today have an average expected longevity of approximately 67 to 69 years, depending upon whether they be boys or girls In brief, in the 50 years of elapsed time from 1900 to 1950, average length of life will have been extended over 20 years There are now more than ten million people over 65 years of age in the United States The differential between men and women is such that it is estimated there were one and a half million more women than men eligible to vote in our 1948 elections The average married woman may anticipate about eight years of widowhood, partly because she will live longer than her mate and partly because she has married a man several years her chronologic senior

Obviously, this advance in age will be slowed, for much of this significant change is attributable to reduction of infant mortality, but there is ample evidence to indicate that it will continue Conservative estimation by the United States Bureau of the Census, assuming no net immigration or emigration, predicts that by 1980 approximately 40 per cent of our population will exceed 45 years of age Of these, nearly 20 per cent of the total United States population will be of the two decades from 45 to 64 These are the critical years, for it is in early senescence that the

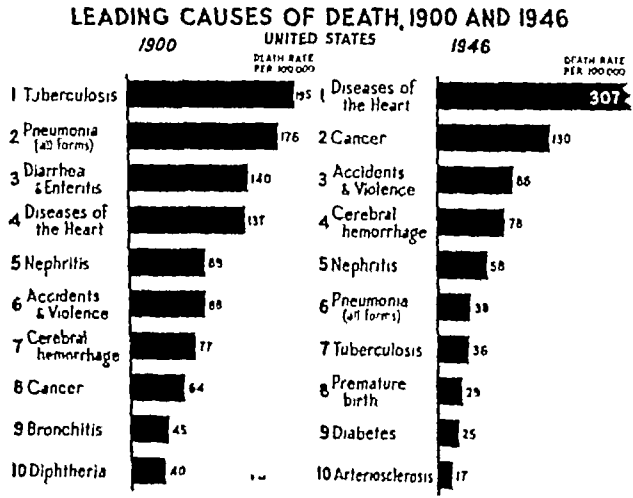

Fig 135 —(Statistical Bulletin, Vol 29, No. 4, Metropolitan Life Insurance Company)

chronic progressive diseases of later maturity first manifest themselves with rapidly rising incidence and an appalling total of disability

Data regarding the shift in emphasis in causes of death are equally dramatic A recent comparison (Fig 135) of the ten leading causes of death in 1900 and 1946 tells an important part of the story quickly and simply Unfortunately, the chart does not combine the closely related vascular disorders behind several of the stated causes of death certainly arteriosclerosis is the true cause of cerebral hemorrhage and of much of the heart disease, diabetes mellitus and nephritis If these entities, all having the common denominator of arterial disease, are combined,

arteriosclerotic disease contributes to the death of 460 persons per 100,000 annually!

It is generally conceded that at present more than 60 per cent of all deaths are due to chronic disorders How much more? Analysis of 1948 data, likewise from the Metropolitan Life Insurance Company,[8] indicates that the true proportion is much higher (Fig 136)

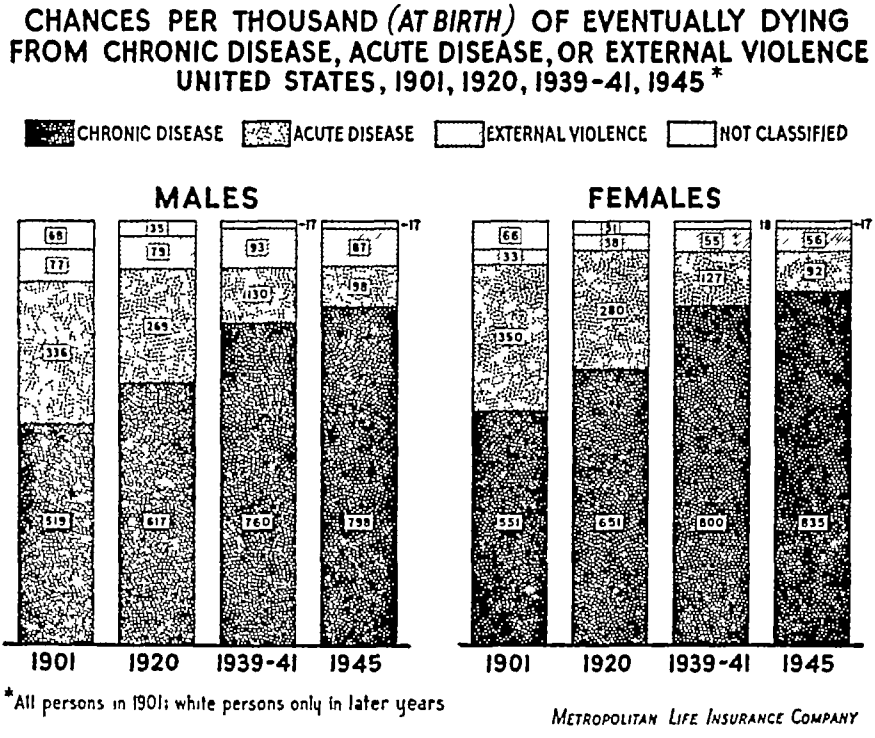

Fig 136

Profoundly impressive as these figures are, they still fail to reveal the full present and impending significance of long-term illness in the health problems of today Mortality data, viewed alone, can be most misleading Morbidity, degree of disability, and duration of chronic invalidism are equally important criteria [9] Data regarding the incidence of the various long-term disorders are few and, for the most part, unsatisfactory Much information is now being accumulated regarding tuberculosis through mass surveys But all previous estimates of the prevalence of vascular disease, diabetes, arthritis and the like are grossly misleading in that they revealed, at most, only the known, discovered, diagnosed cases in which symptoms of sufficient intensity to demand clinical attention were already manifest Certain recent studies indicate that there may be as

many as two million diabetics in the United States, *at least half of whom are unaware of their illness* The number of impending, potential or borderline cases is even larger In many respects, the *undiscovered* cases represent the greater challenge to the medical profession, for the earlier in the course of the chronic progressive disorders therapy is instituted, the better the chances of significant accomplishment This is obviously true of malignant neoplasms, it is equally applicable to arteriosclerosis, hypertensive disease, the aplastic anemias and the arthritides

Total invalidism involving bed or institutional care represents but a small fraction of the total load of disablement, dependency, suffering, lost productivity and economic loss engendered by long-term illness The loss from partial impairment is incalculable [10] The losses due to impairment of efficiency of personnel *not sick enough to be absent* but who accomplish but a fraction of their potentiality because of chronic impairment of health (anemia, hypertension, neglected cholecystitis and so forth) are probably many times more than those attributable to actual time lost [11] As yet, it has been impossible to measure such waste in human productivity as the extent of *total* invalidism was determined by the National Health Survey of 1935–36 [12] A sample of three million people was studied The estimated number of invalids totally and probably "permanently" disabled by long term illness was

Mental and Nervous Diseases	invalided 260,900 persons
Circulatory Disorders	invalided 205,100 persons
Joint Diseases	invalided 147 600 persons
Asthma	invalided 29,200 persons
Renal Disease	invalided 13,600 persons
Malignant Tumors	invalided 28,100 persons
Tuberculosis	invalided 77,900 persons
Diabetes Mellitus	invalided 34,300 persons

The sociologic importance of long term illness needs no further emphasis Longevity is here, but not longevity associated with continued health, vigor and usefulness Long term illness is the most urgent, most important and most complex problem before medical science and practice today It is intimately and inseparably related to age change and geriatric medicine [8] Though chronic illness may arise and disable in youth, most of the invalidism disablement and deaths occur in the years of later maturity Thus two facets of the total problem are involved the fundamental characteristic of chronic diseases, and the basic changes of aging of the patients in whom these occur We must not attempt to divorce the disease from the patient Successful prevention control and cure of long term illness depends more upon management and guidance of the patient whose health is impaired than upon therapy directed

specifically against his disorder In other words we must treat the patient, not merely the lesions of his disease

CERTAIN CHARACTERISTICS OF CHRONIC DISEASE

The most common and significant of the long-term illnesses are those commonly designated by the term, "degenerative diseases" These include four major groups circulatory disorders, metabolic disorders, malignant new growths, and the arthritides A much simplified classification shows some of the more pertinent relationships of these disorders

A Circulatory disorders
  1 Chronic infective myocardial disease
    (a) Rheumatic
    (b) Luetic
  2 Hypertensive arterial disease
  3 Arteriosclerosis
    (a) Cerebral apoplexy
        dementia
        encephalopathy
    (b) Coronary cardiac disease
    (c) Renal chronic nephritis
    (d) Pancreatic diabetes mellitus
    (e) Extremities gangrene
        Buerger's disease
  4 Combination forms
B Metabolic disorders
  1 Diabetes mellitus
  2 Anemia
  3 Climacteric, female and male
  4 Gout
C Malignant tumors, all forms
D Arthritides

Of these, the first two groups, the circulatory and metabolic disorders, are preeminently important They are so intimately related that attempts to separate the consequences into distinct and isolated disease entities are futile [13] It may be worth while to briefly consider some of their generic characteristics, for these affect practice and research alike

Silent Onsets —All these disorders begin asymptomatically and may be well advanced before subjective complaints of sufficient intensity arise to cause the patient to seek medical assistance To be discovered early enough to accomplish much therapeutically, they must be searched for in apparently well people In almost no instances are the symptoms directly referrable to the organic lesions There is no kinesthetic sense which informs of hypertension, arteriosclerotic change induces symptoms only through functional impairment of parenchymatous tissues due to

histanoxia Thus, early detection (essential for early therapy) involves functional evaluation of reserve capacities Depreciations in reserve capacity (cardiac, renal, metabolic) can be detected only by stress tests, unless the depreciation be so great that it is usually irreparable and irrevocable The lesson to be remembered is that we must search for these silent, insidious, fifth column disorders in apparently well people and not wait until they become obvious by overt lesions Health is always relative and the borderline between health and disease vague and indefinite [4, 5]

Multiple Etiology —None of these disorders arises from a single cause They are largely endogenous Superimposition of an accumulative series of insults and injuries is the rule In no two instances is the etiologic background necessarily identical No one will ever discover "the cause" of hypertensive disease, arteriosclerosis or cancer, for there are many causative factors and they vary in each case The concept of specific etiology, so finely phrased by Koch in his postulates and blindly followed by generations of bacteriologists and clinicians, has retarded progress in etiologic analysis for many years Causation always involves three groups of factors predisposing, provoking and perpetuating influences The relative weight of these factors varies in different diseases and in different instances of the same disease For example, perpetuating forces are immeasurably significant in the complex riddle of cancer, for the greatest obstacle to curative therapy is the diabolically persistent continuation of growth and metastasis Similarly, in hypertensive disease the perpetuating influence of medial hypertrophy is a potent antagonist to effective therapy [14]

Awareness of the multiplicity of etiologic factors, their chronologic sequence (provoking factors may no longer be evident when the patient is seen, long after the onset of his long term illness), duration, variability, and the role of constitutional vulnerability [15] (predisposing) is essential to the solution of the vexatious problems of prevention, control and/or cure It is significant that certain factors may contribute to the causation of several of the degenerative processes

Progression —All of these disorders tend to progress Their progression is frequently very gradual but its inevitableness must not be forgotten In no instance is there a significant tendency toward a self-limitation of the disease or spontaneous cure This characteristic of slow but persistent progression is most significant from the point of view of therapy In the first place, because progression is slow, it gives us ample opportunity for complete and thorough diagnostic analysis of all causative influences early in the course of the disease Early in hypertensive disease diabetes, or in arthritis there is no immediate or dramatic jeopardy However, just because of the silent asymptomatic onset

these disorders are rarely identified early in their course Late, when symptoms have become obvious and the patient is already partially disabled, effective therapy is extremely difficult Though there is no immediate haste in the early stages, it is important not to waste this precious time and wait until disability has appeared

Chronic or long-term disability, whether partial or so-called complete may be of one of two types Disability may be progressive or it may be stationary Progressive and increasing disability is to be expected in the degenerative disorders which we are discussing at the moment, and which were listed above However, stationary disability is also a problem of long-term illness By stationary disability we mean the type of situation which arises when an individual has suffered, for one reason or another, an amputation, loss of an arm, has become deaf, or the like The disability of poliomyelitis is relatively stationary It is significant that the handicap from nonprogressive disability diminishes as times goes on because the individual learns to adapt himself to the handicap For example with loss of vision in one eye the individual is a better risk from the point of view of accidents five years after the loss of his eye than he was in the first six months He has learned to look both ways in crossing the street and to adapt himself to his handicap On the other hand, the degenerative disorders, such as hypertensive disease, even if discovered early before there is any actual impairment of function, tend to be progressive and disability is certain to increase as time goes on

In this connection, it is important to point out that in the management of chronic progressive disorders, as well as in stationary disorders, the motivation for improvement is of vital significance The individual with long-term illness will make strenuous effort to improve his health only if there is adequate motivation for so doing People will not make an effort to jump out of an uncomfortable frying pan until such time as they can see a place to land which seems to be more comfortable than where they are The handicapped individual will not exert himself toward rehabilitation if there is no place in society where he may find the satisfaction of usefulness Rehabilitation is impossible without effort on the part of the patient, effort will not be expended without adequate motivation supplied by the promise of greater happiness The management of long-term illness involves sociologic and economic questions as well as purely clinical therapeutics There is serious hazard in making the facilities or institutions devoted to the care and improvement of long-termed sick too desirable or too comfortable Disability of any form must not be a source of profit or satisfaction [16]

Superimposition of Chronic Disorders—More frequently than not, the mature or elderly patient suffers from more than one chronic progressive degenerative disorder These disorders do not confer immunity

to their related diseases, but rather increase the vulnerability of the individual A well known example, often ignored, is the relationship of obesity to the development of diabetes in later years Arteriosclerotic vascular disease, by impairment of nutrition of the cerebrum, is a most significant factor in many of the mental disorders of later years These mental disorders, beginning insidiously with slight distortions of personality, not infrequently lead to abnormal dietary habits and therefore slowly engender deficiency states which may be revealed only much later by anemia and other objective evidences of malnutrition It is extremely important to keep in mind that in the presence of any circulatory handicap, whether it be due to arteriosclerosis, hypertension or cardiac impairment, the coincident existence of even a mild degree of anemia greatly increases the inefficiency of the circulation In a younger individual with normal and elastic vessels, compensation by an increased blood flow is possible, the rigid, tortuous and elongated vessels of the older person cannot so compensate The effects of these various degenerative disorders on the parenchymatous tissues overlap to such a degree that the consequences of impaired function usually do not reveal all the sources of injury [13]

Individual Variability—Great variation is typical of the symptomatology, rate of progression, and severity in individual instances of the degenerative disorders In part this is due to the nature of the disorders themselves and their variable etiology, and in part to the fact that they occur most frequently in older people Individualization in therapy is imperative Routine procedures, whether they be applied in diagnosis or therapy, are sure to lead to poor clinical results Each and every instance of long term illness must be treated as a research project and therapy must be directed toward the improvement of the health of the unique individual

CERTAIN PERTINENT CHARACTERISTICS OF AGE

The problems of long-term illness and geriatric medicine are not identical, though they overlap Except for such disorders as tuberculosis, syphilis, poliomyelitis, orthopedic defects, rheumatic fever and schizophrenia, almost all of the chronic diseases which constitute the immense burden upon society are intimately associated with senescence Their incidence rises sharply after the age of 40, and the phenomena of senescence contributes to their progression Therefore comprehension of the biology of senescence is requisite for proper management and prevention of these disorders [8]

To age is to change The changes of age are not entirely and solely due to the passage of time, for they are effected by the innumerable insults

and injuries which are inevitable in any active and vigorous life It is impossible to distinguish between the depreciations which occur in older individuals as being due to aging as a pure phenomenon and to the scarring and injuries of previous infections, intoxications, traumas, emotional turmoils, fatigues and the like The structural, functional and psychologic changes which occur with aging, even in the absence of known or demonstrable disease, are significant in the management of chronic illnesses Obviously it is impossible to discuss these here at any great length, but a few of the more significant phenomena which occur with apparently normal aging are worthy of brief mention

With advancing age, reaction to injury becomes less vigorous and less rapid As the great majority of clinical symptoms and signs arise as a result of the reactions of the organism to injury, rather than being due to the injury directly, it is obvious that in older individuals symptoms and clinical phenomena are much less conspicuous Clinicians dealing with older individuals must learn to look for minor and subtle changes rather than expect acute and dramatic phenomena In an older patient the febrile response to infection is often minimal It is not unusual for an elderly man to be ambulatory and with a maximum temperature of 100°F in the presence of lobar pneumonia Phenomena such as pain and rigidity in acute appendicitis are often lacking, too frequently the dearth of acute signs in the aged engenders dangerous delay The relative absence of dramatic and distressing symptoms constitutes a dual obstacle to good medicine patients wait too long before consulting a physician and the physician faces a more subtle diagnostic problem Minor variations in the frequency of bowel evacuation, in the character of the stools, and in the amount of effort involved in their passage may be the only symptoms of a nepolasm of the colon or sigmoid at the time when it is sufficiently localized that surgical removal can be complete

Secondly, it must be kept in mind that repair following injury is slowed by age It is well known that the union of fractures in the aged is slow, but it is often forgotten that a similar retardation in the processes of repair follows other injuries, such as infections Prolonged convalescence following an acute infection, whether it be a virus pneumonia or a pyelitis due to prostatic obstruction, must be anticipated Prolongation of convalescence may avoid much permanent irreparable damage consequent to acute disorders, and thus assist in preventing accelerated progression of chronic illness However, just because convalescence takes more time does not mean that the aging individual must be kept strictly in bed It has been demonstrated repeatedly that early ambulation leads to far better clinical results in surgery in older individuals The increase of activity during convalescence should be very gradual,

though progressive It is often convenient to explain to the aging or aged patient that the return to normal levels of vigor from the depletion of illness is not dissimilar to the training of an athlete to supranormal levels of vigor The athlete training for a marathon run does not go out and run the full distance on the first day of his training, he joggs around for a half hour or so to limber up, and then each day does just a little more than on the day before The same principle applies to the convalescence of older individuals

Though the ranges of almost all the "physiologic constants," such as temperature, pulse rate, concentration of glucose, protein, chloride, calcium and the like in the blood, are about the same at 80 as at 8, the ability to maintain constancy of these many equilibria depreciates with advancing age Tolerances for stresses of all sort are diminished, older individuals cannot adjust as well as younger adults to extremes of temperature, dehydration, starvation, excesses of carbohydrates, and the like Acute illness may create stresses that exceed the limited tolerances and so induce decompensation Thus, chronic illness may be discovered during and because of acute illness For example, a mild diabetes may be so aggravated by an acute infection that it first becomes sufficiently manifest to be noted then The clinical function tests involving stress, such as the glucose tolerance test or the renal concentration test, are particularly valuable in detecting depreciations before they are so extensive that they become obvious

Because of lessened homeostatic efficiency, the older patient has a much narrower margin in tolerating functional stress Thus, the effects of any functional impairment are more serious, compensation for one deficiency by another physiologic mechanism is weakened For example, both the aged and the very young are made very ill by dehydration Anemia, even of moderate or slight degree, has more serious consequences in the elderly arteriosclerotic individual than in a young person with elastic and resilient arteries The cardiac load of obesity may be carried by a young myocardium, but the extra work involved in carrying overweight in later years may mean the difference between cardiac competence for reasonable activity and true heart failure Treatment of the aged must neglect no detail in trying to bring weight, hemoglobin, blood protein, blood sugar, and the like to optimum levels

Certain drugs are poorly tolerated by the aged All the barbiturate sedatives are likely to excite and confuse the aged Disorientation forgetfulness, unsteadiness and apprehension are more often enhanced than diminished Bromides, and potassium thiocyanate, often prescribed indiscriminately for hypertensive individuals frequently accumulate because of impaired renal elimination and lead to serious in

toxication It must not be forgotten that bromidism is often associated with excitation, and that further ingestion of more bromide ions aggravates the condition Paraldehyde is a safe sedative for aged patients

On the other hand, tolerance for the nitrites (sodium nitrite, amyl nitrite, bismuth subnitrate and the alkyl nitrates, glycerol trinitrate, erythrol tetranitrate and mannitol hexanitrate), alcohol and the opiates is increased Tolerance for caffeine and/or tobacco is variable, individual variations appear to be independent of age Alcohol in moderation is an extremely useful ajunct in the management of the aged

Habits, good, bad or indifferent, are acquired and fixed by repetition over a period of time The element of time is absolutely requisite Therefore, age is a significant element in habit formation Habits of eating, smoking, sleeping, exercise, alcohol and so forth become fixed in the aged It is important not to insist upon abrupt changes in the habits of aged patients They can be modified slowly and gradually, but abrupt and radical changes in the mode of life are physically upsetting as well as emotionally disturbing Furthermore, if the advice anent habits is too restrictive, the patient will not follow the therapeutic suggestions and nothing whatever is accomplished

Chronic illness progresses more slowly in the aged than in younger persons This is one item on the credit side of the ledger Therefore, the age of onset is an important criterion in evaluating the prognoses of the long-term degenerative disorders Hypertensive disease arising after 60 is usually a much milder, slowly progressive disorder than when the onset occurred ten to thirty years earlier in life [14] Malignant tumors, likewise grow more rapidly and metastasize more quickly in younger patients Similarly, diabetes mellitus in youth is a more critical illness than in later senescence

These are but a few of the factors associated with aging which affect the diagnosis, management and prevention of long-term illness in later years There are among these others which could be considered but lack of space does not permit elaboration It must not be forgotten that in considering the problem of long-term illness we must not be concerned only with the illness, but should be even more interested in the patient who has the illness The emotional outlook to partial disability, the ability to adapt to handicaps, the intensity of motivation for getting well, the purposefulness of existence, the attitude of the family hovering about the chronic invalid, and the attitude of the public toward partial disability are all factors which are of considerable importance in the rehabilitation of those who are but partially disabled Disability is rarely truly total

Long-term illness emphasizes more than any other area of medical practice the relativity of health For several hundred years doctors have

been indoctrinated with the concept that the primary functions of the physician are to discover, identify and treat disease It is our earnest conviction that this attitude is no longer adequate and its continuation can but retard progress of medical science and practice Health is, and should be, something much more than the mere absence of disease Health, being relative, can always be improved No one attains absolute, perfect, ideal health Therefore, if our concern as clinicians were to be focused more upon the construction of greater health of the individual as a whole, rather than merely upon the amelioration of some disorder, it is my opinion that our therapeutic and preventive accomplishments would be tremendously enhanced Unfortunately the realm of preventive medicine has been associated almost solely with the public health activities and the role of the individual, personal, physician patient contact in constructing health has been long neglected [4] There is urgent need for a better comprehension of the positive meaning of health and for clinical methods of evaluation and measurement of health, as contrasted to the identification of disease

SUMMARY

Long term illness, and particularly long-term illness with progressive disablement, is the greatest challenge before the medical profession today This immensely complex problem is intimately associated with the increased longevity of the population The science of gerontology, and its practical clinical application in geriatric medicine, cannot be divorced from the problems of long-term illness Immense progress has been made in enhancing longevity An age of age is here But far too many mature men and women are handicapped, rendered relatively useless doomed to parasitic existence and made miserable by long-term illness

The task before us is to create health to correspond with duration of life Life is multidimensional to be full and rich, it must have depth and breadth as well as length The potentialities of a healthy, vigorous and mature mankind are immense, though as yet largely unexplored Wisdom and judgment are conditioned by age for their development is dependent upon individual experience, which requires time Culture which is the composite judgment and sense of values of a race, nation or group, matures along with the population from which it is derived There is true hope in a more mature future culture, for maturing mankind should become finer, wiser and more tolerant Such maturity, possible only with health into later years may even give to the world a lasting peace Though this goal is yet far off, it is surely worthy of the greatest effort on the part of all of us

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HYPERTENSIVE VASCULAR DISEASE ITS CLINICAL COURSE, DIFFERENTIAL DIAGNOSIS, PATHOGENESIS AND TREATMENT

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INTRODUCTION

Definition.—Hypertension is defined as elevation of systolic and/or *diastolic* blood pressure above a given arbitrary level, set usually at 150/90 or 140/90,[1] based on a statistical survey by the American Heart Association Since isolated systolic hypertension, such as occurs in arteriosclerosis, aortic regurgitation and hyperthyroidism, is of little clinical significance, it is the increased diastolic pressure which is of chief importance However, it should be emphasized that even this is only one sign of a generalized disease or diseases with many other manifestations

Classification —Diastolic hypertension with or *without equivalent* systolic elevation is found in the following conditions

1 *Organic Renal Diseases* Diffuse glomerulonephritis, pyelonephritis, polycystic disease, hydronephrosis, amyloid contracted kidney, diabetic glomerulosclerosis, renal arterial or venous occlusion, and aberrant renal artery

2 *Diffuse Vascular Disease* Periarteritis nodosa, disseminated lupus erythematosus, and thromboangiitis obliterans with visceral involvement

3 *Endocrine Gland Hyperplasia or Neoplasia* Pheochromocytoma, adrenal cortical tumors, ovarian tumors *and pituitary basophilic* adenoma (Cushing's syndrome)

4 *Specific Toxemia of Pregnancy*

5 *Coarctation of the Aorta*

6 *Intracranial Disease* Brain tumors, trauma and infection of the brain stem

7 *Essential Hypertension* (The *condition* in the large majority of cases in which no specific etiologic agent can be demonstrated)

Incidence —There are no adequate published statistic on the incidence of hypertension in the general population Insurance data, which are based usually on single blood *pressure measurements* primarily in men, certainly are unsatisfactory, whereas in the often quoted figures of Master and his associates[2] there is no differentiation between essential hypertension and arteriosclerosis However on the basis of data ob

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tained from large industrial companies, hospitals and old age homes, it has been established that 40 to 50 per cent of the adult population older than 40 years has hypertension Between the ages of 20 and 40 the incidence is about 15 to 20 per cent Although some series quote a slightly greater incidence in women, particularly noticeable during the menopausal decade, there is no true sex difference No definite relation has been demonstrated between spontaneous or castration menopause and the incidence of hypertension [3, 4]

Natural History.—The course of essential hypertension is variable and unpredictable Prognosis is more favorable for a woman, in whom the tempo of the disease is usually slower, the incidence of degenerative vascular complications lower, and the life expectancy greater In about 60 to 75 per cent of hypertensive patients death occurs from cardiac causes—congestive heart failure and myocardial infarction In another 15 to 25 per cent, death results from cerebrovascular accidents—subarachnoid hemorrhage, intracerebral thrombosis or hemorrhage, and fewer than 10 per cent die in uremia [3]

At present it is impossible to predict the course which hypertensive disease will take in a particular patient It may be relatively benign with nearly normal life expectancy, or the disease may become accelerated with death in a few years or even months However, in a recently reported series of private patients, Burgess[5] found that life expectancy could reach within three or four years of normal if the diastolic pressure persisted at 100 or over for eight years without signs of renal or cardiac disease However, the younger the patient when hypertension is discovered, the less likely he is to fulfill his normal life expectancy In patients of age 50 and below, with diastolic pressure over 100 mm Hg, the average survival period is over fifteen years, about eleven years below the normal expectancy

CLINICAL COURSE

Essential Hypertension.—Hypertension may be present intermittently or constantly for years or decades before symptoms appear However, there may be a long history of antecedent or concurrent complaints dependent on autonomic instability as shown by cardiovascular and gastrointestinal irritability, migraine, fatigability and allied disorders [3, 6–9, 11–17, 23] Such disorders are probably a function of the aggressive, dependent, emotionally labile personality pattern frequently found in the hypertensive and may be precipitated or exaggerated by the patient's discovery of the hypertension The benign period of hypertensive disease terminates when some part of the cardiovascular, cerebrovascular or renal vascular reserve is taxed to the point of insuffi-

ciency The incidence and frequency of physiologic decompensation varies tremendously Multiple system breakdowns are of common occurrence, once any system yields This is to be expected from circulatory interrelations Factors such as acute infections, diabetes, physical or emotional stress, and the unknown process of aging play a significant accelerator role [2, 6, 9, 10, 12, 18–22, 27] A major surgical procedure, pregnancy or the pyrogenic reaction of an ordinary febrile illness may cause a temporary fall in blood pressure, but such transient alleviation does not preclude later aggravation which may or may not be related to the traumatizing experience [15, 15, 24–26]

Cardiac Symptoms —After either a prolonged period of moderate, or a shorter period of severe, hypertension, 60 per cent of the patients develop asymptomatic left ventricular hypertrophy and/or aortic dilatation or elongation [3] A hard flat pulse, a snapping, ringing second aortic sound, and a forceful apex beat are common findings [6, 18, 27] Occasionally, systolic murmurs at the apex or base and, infrequently, diastolic murmurs at the aortic area, which must be differentiated from *sounds* resulting from arteriosclerosis or other coexistent heart disease, are heard Episternal pulsation, due to lifting of the innominate artery by an elongated aorta, is noted frequently in patients with prolonged hypertensive disease [3]

A few patients, particularly with pre-existent heart disease, *go into* failure before clinical evidence of hypertrophy is present. A few never reach the point of failure In the remainder, with varying degrees of hypertrophy, decompensation may supervene at any time Fatigue and moderate dyspnea on effort common earliest symptoms of left *ventricular* failure are present in 40 per cent of the patients by the time hypertension *is discovered* At first examination other complaints may be cardiac arrythmias in 25 per cent of the patients, *cardiac pain in 20* per cent, congestive heart failure in an occasional patient, and paroxysmal nocturnal orthopnea or acute pulmonary congestion in a rare one [3, 6, 10, 27, 28]

Patients with early heart failure usually present evidence of *left* ventricular dilatation superimposed on the *hypertrophy* *The* dominant second aortic sound is lost as a loud second pulmonic sound develops Mild *tachycardia*, transient gallop rhythm, and often functional apical systolic murmurs may be present It is in this group of patients, and particularly in those with very high diastolic tensions, that paroxysmal pulmonary edema, with its acute terror, suffocating, dyspnea cyanosis and "strawberry" froth, is seen However, dramatic though these attacks may be they rarely last over an hour frequently subside spontaneously, readily respond to treatment, and in hypertensive disease are an infrequent cause of death [3, 11, 21]

With the onset of systemic congestion which follows in 87 per cent of

the cases, the signs due to pulmonary congestion may subside, but the incidence of cardiac arrhythmias increases and some 10 per cent of the patients may develop auricular fibrillation These arhythmias are not inconsistent with a good prognosis except for persistent pulses alternans and gallop rhythm,[18] which usually indicate a life expectancy of not over two years For the rest, the signs and symptoms are those of heart failure from any heart disease, with dyspnea, orthopnea, cyanosis and edema Death usually occurs within two to four years for 67 per cent of the men and 50 per cent of the women, and within ten years for nearly all of the men and most of the women Myocardial infarction may occur at any time in the course and contribute to the onset of heart failure, and in 10 per cent of the cases it may directly cause death [3, 6, 18, 20, 27 31]

Cerebrovascular Symptoms—Second in importance in the clinical picture of hypertensive disease are the cerebrovascular symptoms These increase in incidence with the duration of hypertension so that, although present in only 67 per cent of the patients at the time of discovery, they are much more frequent ten years later An early, and sometimes only, complaint is headache or dizziness Later, nervousness and insomnia assume equal proportions Depression, tinnitus and actual cerebral accidents are unimportant at first, but after several years they may occur in 5 to 10 per cent of the patients The course in this type of case is rapid, and death from a cerebral accident commonly occurs in 25 per cent of the patients in two years and in 75 per cent in five years [3, 18, 19, 27 31]

Hypertensive encephalopathy, with its picture of papilledema, elevated spinal fluid pressure, persistent severe headache, vertigo and syncope, nausea, vomiting, visual disturbances, and occasionally convulsive or hemiplegic phenomena, is rare When it occurs in hypertensive disease, it is commonly in a patient with long-standing hypertension, it may be marked by an additional elevation in blood pressure and frequently indicates onset of the malignant or accelerated phase of uremia It is nearly always associated with organic changes in the brain [30] Hypertensive encephalopathy, however, although offering a poor general prognosis, does not show a high correlation with death by cerebral accident [5, 18 31 33]

Renal Symptoms—Uremic deaths in hypertension occur with relative infrequency Terminal glomerulosclerosis and primary malignant nephrosclerosis each represent 1 or 2 per cent of necropsy material Terminal glomerulosclerosis, clinically and pathologically, represents the renal failure of essential hypertension Malignant hypertension or malignant nephrosclerosis is fundamentally different in its vascular pathology, although it may appear to be just an exaggeration of the "essential" process With the necrotizing arteriolitis there is an acceleration

in the progress of the disease, usually an increase in the arterial tension and in the renal, retinal and cerebral symptoms, and a general morbidity not seen in benign hypertension Malignant hypertension may occur as an apparently isolated phenomenon, but it is more commonly superimposed on a pre-existent hypertension of some other type [2 13 18 21 28]

A pathologic condition of the kidneys, in the form of pyelonephritis, urolithiasis, acute or chronic glomerulonephritis, hydronephrosis, or any of the congenital renal anomalies, is present in about 20 per cent of the patients with hypertension when the hypertension is discovered, and some pathologic condition develops with varying degrees of renal functional impairment in many more before death results from some other cause This group of patients, most of whom are in the younger age range, contributes the remaining percentage of uremic deaths [2 22 24] Hypertension following the toxemia of pregnancy can be included in this group of conditions, with the prognosis dependent on the presence or absence of renal complications such as nephritis or pyelonephritis [25 26 31 35]

The onset of uremia commonly is heralded by visual disturbances due to malignant retinopathy Fatigue, torpor, loss of weight, anemia, anorexia, nausea, vomiting, headache and pruritus may occur The subsequent course is well known Death may ensue in a matter of days, weeks or months, rarely, after remission, it occurs in one or two years [18]

Retinal Symptoms—Hypertensive retinopathy is frequently considered an index of the severity of the hypertensive disease The more proper association should be with the severity of the arteriolar involvement, which need not parallel the increase in diastolic blood pressure Retinal changes usually do not occur until after at least five or ten years of persistent hypertension and correlate poorly with the general prognosis, unless they are extreme [2 12 19 26 27]

Secondary Hypertension—Up to this point, our main consideration has been the clinical course of the ordinary or "essential" hypertensive disease The picture is somewhat different in the secondary types of hypertension, owing to the predominant effects of the underlying major disease

Arterial Disease—Arteriosclerosis, which has a high incidence in hypertensive patients, contributes materially to the course of circulatory, cerebral and renal pathologic changes, and adds specific peripheral vascular complaints to the picture in the older age range The blood pressure elevation, due to the loss of arterial elasticity, is principally the systolic rather than in the diastolic phase Angina pectoris coronary occlusion are frequent complications [2 13 33] In diffuse ob[illegible] tive vascular diseases with which hypertension [illegible] particularly when the renal vessels are involved, the [illegible] are predominantly those of the vascular lesion [illegible]

tension [18, 22, 39] Thus, in thromboangiitis obliterans and arteriosclerosis obliterans, the course is one of peripheral involvement with thrombosis, ulceration, amputation and intercurrent infection In thromboangiitis obliterans, the patients are young, and there are widespread involvement, local perivascular inflammation, severe pain and a relapsing course In arteriosclerosis obliterans, the patients are older, vascular involvement is chiefly in the lower extremities, and, unless accelerated by diabetes, the process is apt to be chronic and indolent, with death from heart disease or some other product of general aging In both of these conditions, hypertension, when present, may partially counteract the vascular insufficiency In periarteritis nodosa, lupus erythematosus and subacute bacterial endocarditis the panarteritic involvement may frequently produce a picture clinically similar to that of rheumatic fever or glomerulonephritis, and may be mistakenly diagnosed as such unless specific diagnostic criteria appear [39, 40]

Coarctation of the Aorta —In the rare case of coarctation of the aorta, the high cephalad tension and cardiac strain may result in early death from cerebral accident or congestive failure If the constriction is not too severe, the course may be similar to that of ordinary "essential" hypertension The hypertension in these congenital cases is seen early and is relatively more in the systolic than in the diastolic phase [41, 42]

Endocrinopathy —In the common endocrinopathies, the association of hypertension with obesity and diabetes is well known, but the clinical significance of this correlation is uncertain, except for the increased incidence of arteriosclerosis and cardiac strain seen in these cases [3] In hyperthyroidism and menopause, hypertension is simply coincidental [4, 43] However, in two rare conditions, Cushing's syndrome and pheochromocytoma, both marked by the rapid development of high arterial tension in younger people, the association is specific In the first instance, the hypertension is fixed and associated with striking changes resulting from dysfunction of the pituitary, adrenal cortex, gonads and parathyroids Death from general debility commonly occurs in a few years, although occasionally it may be precipitated by heart failure or uremia [44] In pheochromocytoma, the hypertension is classically intermittent and malignant, so that each attack, although presenting all the signs of epinephrine overdosage, may resemble acute encephalopathy or pulmonary edema Chronic pheochromocytoma, which in its course and termination is extremely difficult to differentiate from "essential" hypertension, also occurs [45, 46]

DIFFERENTIAL DIAGNOSIS

History and Physical Examination —Once a patient has been found to have elevated blood pressure, repeated observations are necessary to

distinguish between transitory and sustained hypertension The patient should return on several occasions and should be put at ease, either by rest or by casual conversation, before the blood pressure is measured Determinations in the more familiar environment of the home may be desirable in doubtful cases [16]

Blood pressure should be measured in both arms and also in the legs on at least one occasion, with the usual precautions in technic [47] The blood pressure level may vary tremendously depending on the mental and physical stresses to which the patient is exposed However, persons who show even transient hypertension are more likely to develop a later sustained hypertension,[48] and should receive continued follow-up Patients who, when put at ease, consistently show a blood pressure over 150/90 on three separate occasions are best considered to have permanent hypertension and should be studied to determine if any condition known to cause hypertension is present or whether they should be classified with the majority group of so-called essential hypertensives

A thorough history and physical examination is of prime importance in the work up of the hypertensive patient This is particularly true for the younger patient, because of the increased incidence of hypertension as a result of certain rare conditions and of renal diseases, some of which are subject to specific therapy

The incidence of hypertension in the patient's family should be ascertained if possible, since there is a strong familial influence Special emphasis should be given to any previous history of hypertension, and the patient should be asked about previous examinations (employment, insurance army, clinic or hospital, etc), when blood pressure may have been determined Such questioning frequently aids in establishing the duration of the disease and is important in cases in which subsequent myocardial infarction may have lowered the blood pressure Information on pre existing renal disease, diabetes or toxemia of pregnancy aids in differential diagnosis

Differentiation from essential hypertension of the hypertension occurring in pyelonephritis and sometimes in nephritis may be quite difficult Once the acute or specific episodes are past, clinical course and urinary findings are frequently so similar that the etiology may not be determined unless there is a definitive history The differential diagno is is important, particularly in estimating the outlook in pregnancy since the mortality is less and the life expectancy greater in essential hypertension [3 5 11 12 34 49]

The patient should be specifically asked about the common symptoms such as headache vertigo, tinnitus, undue fatigue palpitation, dyspnea, orthopnea, nosebleeds and visual disturbances Signs and symptoms of renal disease such as polyuria, nocturia, frequency and urgency, pyuria,

and proteinuria should be carefully elicited Any of the common symptoms that occur in a paroxysmal manner, such as the sudden onset of headache, palpitation, flushing, or sweating, suggests the possibility of a pheochromocytoma

Many hypertensives are obese and stocky, and have a plethoric appearance The general attitude of the patient and the degree of nervous tension should be evaluated Thyrotoxicosis can cause hypertension and great nervous tension, and in this connection examination of the ocular movements is important The ophthalmoscopic examination of the ocular fundus is one of the most important procedures in the physical examination The degree of narrowing, change in the light reflex from the vessel walls, and the presence of hemorrhages, exudates and papilledema may give considerable aid in establishing the severity and prognosis of the hypertension Examination of the fundus should be carried out in a darkened room and with the aid of a mydriatic, and the physician should be as adept with the ophthalmoscope as he is with the stethoscope [12 18 36, 37]

Examination of the heart for evidence of enlargement or presence of murmurs or cardiac arrhythmias described in the discussion of the clinical course is important The lungs should be examined for the scattered rales of early congestive failure One important finding in early congestive failure may be alternation of the pulse on auscultation of the blood pressure

In hypertension due to coarctation of the aorta, a dilated, pulsating intercostal artery can occasionally be palpated, and a murmur may be heard in the interscapular region In this condition the pulse in the legs may be diminished or retarded, and the legs may be underdeveloped

The hair distribution should be noted, especially in women, since certain diseases of the gonads or adrenal cortex that result in hypertension may be accompanied by hirsutism There may also be purplish striae of the abdominal wall The tumor of the kidney, ovary or adrenal cortex that is accompanied by hypertension sometimes is palpable on abdominal examination

This brief account naturally applies more to the patient with asymptomatic hypertension However, hypertension may be first discovered in a patient suffering from full-blown congestive heart failure, uremia or hemiplegia

Laboratory Tests —It is desirable to have certain laboratory determinations made for every hypertensive patient If there are indications that one of the rarer, possibly correctable, forms of hypertension is present, these laboratory aids may be the only means of establishing the diagnosis

In much older patients with hypertension a routine blood count, blood glucose, blood urea nitrogen, chest x-ray, electrocardiogram, and the urinary examinations discussed below are usually sufficient to establish the diagnosis An electrocardiogram may be of great help in evaluating the cardiac prognosis, particularly if signs of left ventricular strain, left axis shift or myocardial infarction are present

A fresh, concentrated, acid urine specimen should be examined The presence of proteinuria, casts or red cells suggests a primary renal disease Abnormal constituents are not prominent in the urine of patients with early hypertension The differentiation between advanced forms of glomerulonephritis and malignant hypertension is difficult, but at times it can be established by quantitative estimation of renal function, by means of clearance and tubular saturation techniques [50]

Estimation of concentrating ability, when properly carried out, is a simple and sensitive test of renal function The urine is collected in the morning, after an afternoon and overnight period of eighteen hours during which no fluid in any form, and no 5 or 10 per cent fruits or vegetables are taken but the patient is permitted the usual solid foods and salt The diet of the previous day should contain only small amounts of fluid, and the patient should void before retiring The specific gravity of the morning urine specimen should equal or exceed 1 024, after subtracting 0 003 for each gram of protein per 100 cc of urine in event of massive proteinuria If the urine is not concentrated to this extent, the test should be repeated unless contraindicated by the patient's condition or reaction to dehydration If the result is confirmed, a more precise measurement of renal function is indicated Determination of the urea clearance is valuable, but for reliable results the urine collections must be accurate

Special Procedures.—Although intravenous pyelography is not necessary in all hypertensive patients, x ray visualization of the kidneys is essential in the young patient and in those who have any symptoms or signs suggestive of disease of the urinary tract Retrograde pyelography may be necessary in selected cases

Any significant renal abnormality disclosed on the pyelogram, particularly if unilateral and in a young person, is potentially the source of the hypertension and, in rare cases, can be "cured" by removal of the involved kidney [51] In such cases separate determination of the glomerular filtration rate (GFR) renal plasma flow (RPF), filtration fraction (FF), and maximal tubular excretory capacity for para aminohippuric acid (T_{max} PAH) for each kidney is advisable The presence of vasopressor substances in blood obtained by catheterization of the renal vein may also supply evidence that one kidney or the other is con

tributing excessively to the maintenance of the hypertension [51] These procedures can be carried out only by teams of experienced physicians at certain specially equipped clinics

The presence of hirsutism, polycythemia, abdominal striae or osteoporosis associated with hypertension suggests the possible presence of a tumor or hyperplasia of the adrenal cortex, ovary or pituitary These sites should be investigated by x-ray after perirenal insufflation with air, or by surgical exploration The urinary excretion of 17-ketosteroids is frequently elevated in this group of patients

The symptoms of a tumor of the adrenal medulla have been described above If pheochromocytoma is suspected, pyelography and x-ray studies of the adrenal, utilizing perirenal injection of air, are useful, but surgical exploration may be the only certain means of diagnosis, particularly in those epinephrine-secreting tumors of chromaffin tissue which are located extra-adrenally Many of these patients have glycosuria and hypermetabolism and are distinguished from hyperthyroid patients only with difficulty An intravenous injection of 0 05 mg of histamine will provoke a hypertensive episode in a patient with pheochromocytoma,[52] but it may be dangerous to use this means of establishing the diagnosis A preferable method is the use of an epinephrine antagonist, such as benzodioxan, which neutralizes epinephrine and produces a lowering of the blood pressure when it is elevated as a result of excess circulating epinephrine [53]

In hypertension due to coarctation of the aorta, the systolic blood pressure is lower in the legs than in the arms, and, depending on the position of the coarctation, there may be a difference in the blood pressure in the two arms The chest x-ray may show "notching" of the ribs due to the erosion caused by the dilated intercostal arteries Diodrast angiocardiography occasionally be desirable to visualize the site of the coarctation before operation designed to correct the defect

Persisting headache or papilledema, especially when associated with neurologic signs in a patient recently discovered to have hypertension, should arouse suspicion of brain tumor, and thorough neurologic work-up, spinal tap and electroencephalogram are indicated

The use of the dibenamine, tetraethylammonium chloride, sodium amytal and cold pressor tests is largely helpful in evaluating the possible effect of sympathectomy on the blood pressure level, but the results are not too satisfactory, moreover, these tests are of little value in the differentiation of one type of hypertension from another [12 21 31 83]

PATHOLOGIC PHYSIOLOGY

Rational treatment must be based on an understanding of the fundamental physiologic abnormalities in disease Therefore, although the

pathologic physiology of hypertension has recently been reviewed elsewhere,[12, 13, 55–57] certain features might well be summarized here

It has been well demonstrated that in practically every type of clinical and experimental hypertension only one of the factors determining blood pressure—peripheral resistance—is increased, since the others—cardiac output[12] and the volume and viscosity[60] of the blood—are within normal limits In certain types of clinical and experimental hypertension, a mechanism producing the arteriolar constriction responsible for the increased peripheral resistance is demonstrable For example, in pheochromocytoma, hyperadrenalism results in marked vasospasm, and in brain tumors increased intracranial pressure results in stimulation of the vasomotor center In diffuse vascular diseases, organic occlusive obliteration of vessels with associated local vasospasm, as well as involvement of the kidneys, is present In coarctation of the aorta, the situation is not clearly defined, but Steele[62] has presented evidence that there is increased peripheral resistance distal as well as proximal to the aortic constriction In Cushing's disease and in overdosage of desoxycorticosterone, the excess adrenal steroids in some way produce elevated tension, whereas in bilateral renal disease renal mechanisms doubtless are responsible for the increased peripheral resistance But the vasoconstrictor factor in what is one of the most important clinical entities in the western medical world—*hypertensive vascular disease*—has not yet been determined

The brilliant investigations of Goldblatt and his associates[51, 52] and the later work of others[53, 54] led to what seemed to be a satisfactory hypothesis which again brought most human hypertensive vascular disease under the control of a single etiologic factor—renal involvement Briefly, the hypothesis is as follows In human essential hypertension, as in its experimental analogue, renal hypertension, some disorder of the renal circulation, possibly arterial or arteriolar sclerosis, leads to the release from the kidney of the enzyme, renin, which itself is not a vasoconstrictor Renin presumably catalyzes the conversion of alpha 2-globulin (renin substrate or hypertensinogen) to an active vasoconstrictor (angiotonin or hypertensin), which produces arteriolar constriction and is destroyed by enzymes (angiotonase or hypertensinase) in the blood and various other tissues[51, 57, 58] The actual stimulus leading to the release of renin is not known, but recent evidence indicates that it is certainly not oxygen unsaturation of the renal blood[59, 60] and that it is not necessarily associated with decreased renal blood flow in dogs with experimental renal hypertension[61] More recently, there has been new interest[64] in the suggestion of Dock[5] that, late in experimental renal hypertension, vasoconstriction may be dependent on a mechanism mesh-

ated through the central nervous system by some humoral stimulation rather than by reflex neural stimulation The significance of this is not yet clear

Although it has been generally accepted that this system may be involved in the hypertension of glomerulonephritis, pyelonephritis, polycystic kidneys, etc, the argument that human essential hypertension results from a primary renal mechanism has been attacked for the following reasons

1 Not infrequently renal blood flow is normal early in essential hypertension, therefore, the later renal ischemia may be secondary to some other factor [12 31, 68 70]

2 Renal arteriosclerosis, or arteriolosclerosis, is virtually absent in many early cases and, consequently, cannot be a primary etiologic factor [12 69]

3 There is no good evidence that disease of the urinary tract or unilateral kidney disease can produce human hypertension [12 34]

4 Renin or hypertensin is not demonstrable in increased quantities in systemic or renal vein blood in benign essential hypertension [57]

Despite these criticisms, the striking parallels between experimental renal hypertension and human essential hypertension leave the issue unsettled Furthermore, new lines of investigation continue to suggest some renal involvement in the genesis of human and experimental hypertension For example, Shorr[56] and Zweifach and Shorr and collaborators[108] have found that the renal vasoexcitor material (VEM) and, to a lesser degree, the hepatic vasodepressor material (VDM), which Chambers and Zweifach[108] first described in connection with hemorrhagic and traumatic shock, are present in the renal vein and systemic blood in increased amounts in different proportions in the several stages of experimental renal hypertension and in essential hypertension in man Evaluation of the significance of these observations as regards experimental and clinical hypertension, as well as of the report by Shipley, Helmer, and Kohlstaedt[72] of a sustained pressor principle in the blood of cats dying from prolonged hemorrhagic hypotension and other causes, must await further experimental confirmation and interpretation

In addition, evidence is accumulating that the kidney in well established essential hypertension may not be functionally normal Farnsworth[73] first reported an increased chloride clearance with water diuresis in hypertensive subjects without "obvious" renal disease Many of her patients, however, had poor kidney function, in view of their low glomerular filtration rates In a small but well controlled series we[74] have found that hypertensives with good renal function, as demonstrated by fairly normal glomerular filtration rate and Tm_{PAH}, on full and low

salt diets, exhibit the same abnormal parallelism between water, sodium and chloride excretion during water diuresis The locus or nature or significance of the pathologic process involved is not clear However, this may be the most sensitive index of renal dysfunction in hypertension yet described

Adrenal cortical steroids apparently are involved in the genesis and maintenance of hypertension Adrenalectomy abolishes or prevents the development of experimental renal hypertension or the production of vasoexcitor material by dog kidneys when incubated anerobically in vitro[64, 65] Selye[70] produced hypertension and nephrosclerosis in experimental animals by administration of adrenal steroids or anterior pituitary corticotrophic hormones, or as part of the general adaptation syndrome at a stage when adrenal hypertrophy and hypersecretion were present These effects can be exaggerated by high protein, high salt diets, and prevented by low salt or low protein diets or the administration of acidifying salts such as ammonium chloride which promote sodium excretion

The relations of these observations to human essential hypertension are not clear Despite the evidence of Perera[76, 77] and his associates and of Schroeder[78] of the pressor action of desoxycorticosterone and the evidence of Perera and Blood[73] of salt and water retention in hypertensives, there has been no convincing proof of increased adrenal cortical function in any types of human hypertension other than in that observed in Cushing's disease

It has been contended that different endocrine glands may be involved in human essential hypertension For example, some[79] have argued for increased posterior pituitary activity and others[80] for depressed posterior pituitary function in human hypertension Both theses are highly hypothetical The factors regarding "blast hypertension"[37] are still unevaluated

Thus, despite extensive clinical and experimental investigation the cause of human essential hypertension is unknown As attractive and simple as the renal pressor hypothesis may be, it must be recognized that its importance in the human clinical syndrome is as yet unproved and in fact is seriously in doubt Some[21, 5] have presented arguments for a primary neurogenic origin of the hypertensive process, despite the demonstration by Pickering[61] Prinzmetal and Wilson,[62] and Stead and Kunkel[19] of the minimal contribution of neurogenic factors in hypertensive vasoconstriction But the knowledge whether the initiating mechanism and the sustaining mechanism are identical, whether either is neurogenic or humoral and whether the hypertension and the arteriolosclerosis may not both be the result of some unknown underlying vascular disease, must await further study[17]

TREATMENT

Just as the etiology of essential hypertension has been attributed to diverse factors, so has therapy followed complete cycles of enthusiastic acceptance, rejection and rediscovery of innumerable specific and non-specific treatments, none of which have withstood critical analysis With monotonous regularity, re-examination of the spectacular results of some particular treatment reveals poor control or absurdly short pre-treatment observation periods As is well known, many hypertensives will respond dramatically to removal from their accustomed environment and occupation, particularly with hospitalization and bed rest Furthermore, Ayman[84] has noted that blood pressure reduction and/or symptomatic relief can be achieved by superficial psychotherapy, reassurance and enthusiastic acceptance of any treatment for hypertension, including, in his own "experimental" series, 10 drops of dilute hydrochloric acid taken in colored water before each meal It is significant that he found favorable results reported in thirty-five papers on the treatment of hypertension by measures ranging from administration of watermelon extract and thiocyanate to the irradiation of the skull or suprarenal regions

Too often decreased blood pressure has been the sole objective of suggested treatment and the sole criterion of its efficacy, a fact which left proponents subject to the criticism that they were treating blood pressures and not patients Granted that hypertension is only one manifestation of some underlying process, it is still an important index of the increased peripheral resistance, the increased cardiac work, and the strain on the sclerosing arterial and arteriolar vasculature of the afflicted subjects Before sclerotic changes have too greatly compromised important vascular channels, for example the coronary vessels, permanent decrease in blood pressure to normal levels *per se* should be beneficial However, although blood pressure gives an "objective" variable to follow, the effects of specific or general therapy must be evaluated in terms of the natural history of the disease, provided the physician can decide on suitable criteria for this difficult task, involving decades of a patient's—and of the physician's—life

Despite the discouraging outlook, much can be accomplished for hypertensive patients by thorough medical work-up with the assurance of competent medical and psychologic management[85, 86] by an interested and able physician In the usual long period intervening in many cases between discovery of elevated blood pressure and appearance of the first significant symptoms, a great deal can be done in active and prophylactic management, as well as in preparing the patient for his future life

After exclusion of the known causes of hypertension, a proper evaluation of the patient's clinical status must be made Based on the clinical and laboratory studies discussed above, an estimate of the patient's cardiac, renal and possibly vascular status can be made Then, a series of reassuring, confident, but candid discussions with the patient about the nature of his disease and what it means to him should be stated How much or what each patient is to be told must be determined as the physician learns more about him Certain topics, such as the patient's actual blood pressure, the relative insignificance of blood pressure readings *per se*, the physiology of blood pressure regulation, the general course of the disease, life expectancy, etc, must be considered at some time It is particularly important that the physician gradually win the patient's confidence by a fair, honest, but sympathetic presentation of the facts, if the patient is ultimely to gain insight into the nature of his disease and the intimate relation between his emotional state and his ultimate prognosis

In the asymptomatic phase, blood pressure determinations should be de-emphasized and the patient should be taught moderation in diet and activity Weight reduction with a 1200 calorie diet if indicated, frequently brings about a gratifying decrease in pressure[87] Ultimately, in this phase, functional complaints of headache, fatigue and nervousness may appear and respond well to the usual analgesics, sedation, reassurance, or even placebos[87] At this time the patient generally becomes more anxious about his disease, and the more intelligent patient begins to ask questions about the two most highly publicized therapeutic experiments in hypertension, the rice diet and sympathectomy

The therapeutic efficacy of the Kempner regimen,[88] despite the original thesis that a low protein intake could correct some underlying renal metabolic abnormality, probably results from the low sodium content of the rice, fruit and fruit juice diet[89, 90] Thus, it represents a return again to the concept of sodium chloride restriction, first advocated in France by Ambard, who later abandoned it (see Schroeder[91]), and later proposed in America by Allen,[92] who has been urging its more widespread application since 1922

On theoretical grounds, the strongest argument for restriction of salt and protein are the work of Selye[3] discussed above, and the report by Knowlton and her co workers[93] that adequate sodium chloride intake is required for the pressor action of desoxycorticosterone in nephrotoxic-serum nephritic rats If adrenal cortical and other steroids, and particularly desoxycorticosterone, play an important primary or secondary role in the genesis or maintenance of clinical hypertension, rigorous salt and protein restriction seemingly should tend to interrupt the complex process How else these regimens may function is not known[94]

Despite these considerations and the favorable results reported by Kempner and others,[90, 93, 94] with marked reduction in blood pressure, improvement not only subjectively but in eyegrounds and electrocardiogram, and decrease in cardiac size in about 67 per cent of patients placed on a 2000 calorie diet containing 20 gm of protein, less than 0 2 gm of sodium, and 1000 cc of total fluids, carefully controlled observations by most other investigators have not disclosed comparable success[58, 59, 74, 95] in much smaller series of patients The psychotherapeutic influence of both Kempner's vigorous advocacy of deprivation therapy and the mass patient participation program extending over a period of months must not be underestimated in evaluating his results However, the recent analysis by the Minnesota group[96] of the effects of prolonged low calorie and low protein intake in an experimental group of normal men, as well as in a large series of hypertensive subjects during and after the Leningrad siege, indicates that continued drastic food restriction alone may cause slight lowering of the blood pressure in normal subjects and marked improvement in both the blood pressure and the clinical picture in persons with hypertension

A contraindication to this type of therapy, however, has been noted by several investigators,[95, 98] who report that severe or even fatal uremia may develop in patients with poor renal function when they are placed on the low salt diet, particularly when sodium loss is accelerated by concurrent administration of mercurial diuretics The explanation for this phenomenon is probably the significant decrease in glomerular filtration rate and renal plasma flow which occurs in hypertensive patients with good or poor renal function when salt intake is vigorously reduced [74] Another real contraindication exists in the small group of patients with salt-losing nephritis in whom, as is well known, a syndrome simulating adrenal cortical hypofunction may develop when they are placed on a low salt diet [99] In addition, a recent report[100] indicates that not all patients on the rice diet are in nitrogen equilibrium

Yet any hypertensive patient with good or fair renal function should be given the opportunity of trying the rice diet or one of its modifications (see Table 1) Every series, including our own and those of even severe critics of the regimen, contains a small group of patients who unpredictably respond to the Kempner or an equivalent low salt diet with a marked fall in blood pressure, at time to normal levels, with symptomatic improvement Obviously, in patients with evidences of congestive failure, the low salt regimen will often bring dramatic signs of improvement To promote more rapid loss of salt we[74] and others[94] have given weekly or biweekly injections of mercurial diuretics, at times until, as we have reported,[101] the marked drop in glomerular filtration rate, among other factors, renders the patient relatively resistant to these agents

TABLE 1

Modified Rice Diet

Basic Low Sodium Foods

Rice and rice products
Rolled oats, shredded puffed or Cream of Wheat
Sugar honey, jelly, jam
Fruits and selected vegetables
Low sodium milk (Lonalac)
Butter
Chocolate syrup
Coffee, tea
Low salt cookies
Low sodium bread

Sample Daily Menu

Breakfast

1 glass orange juice with sugar
½ cup puffed rice
4 oz. low sodium milk
Sliced banana with sugar
Coffee with sugar

10:00 A M

1 glass pineapple juice
1 pear

Dinner

½ grapefruit
Cooked rice with cinnamon and sugar
4 oz. low sodium milk
Baked potato with 2 pats of butter
Sliced tomato on 1 lettuce cup-lemon
Low sodium bread
Sliced fresh peach with sugar
Tea with sugar

3:00 P M

1 glass apple juice
Peanuts (roasted in the shell)

Supper

1 glass grape juice
Vegetable plate
Corn on cob with 3 pats butter
Green peas
Summer squash
Low sodium bread
Strawberries with sugar
Coffee or tea with sugar

8:00 P M

Fresh apple
1 glass low sodium milk with chocolate syrup

Fruits Permitted

Apples	Grapefruit	Pumpkin
Apricots	Lemons	Quince
Bananas	Orange	Raspberries
Blackberries	Peaches	Strawberries
Blueberries	Pears	Watermelon
Cherries	Pineapple	
Grapes	Plums	

Juices from any of these fruits and salt poor tomato juice may be allowed

Vegetables Permitted

Beans (green and lima)	Okra	Radishes
Corn	Peas	Rutabagas
Cucumbers	Peppers (green)	Squash (winter and summer)
Eggplant	Potatoes (white and sweet)	Tomatoes
Lettuce (for garnish)		

If a patient fails to respond within eight or twelve weeks to the Kempner diet probably no response will be achieved We have observed patients in the hospital in whom administration of the strict rice diet for two to four months produced no detectable change in blood pressure or clinical status, despite weight reduction and starvation to the point of grave weakness As yet, it should be repeated, there has been no evidence presented that any form of low salt or low protein diet can alter the natural history of most cases of hypertensive vascular disease, although such dietary restrictions at times may tide a patient over a vascular crisis Moreover, any improvement obtained, either subjective or objective, still awaits a scientific explanation

The question of sympathectomy is as controversial and confusing as that regarding salt and protein restriction In contrast with the early enthusiastic claims of the surgeons[102–106] as to the results of supradiaphragmatic splanchnicectomy, lumbodorsal sympathectomy or total sympathectomy, more careful evaluation of the several extended series which have since accumulated has given a more realistic if less happy estimate of the results obtained by these procedures The early claims that sympathectomy improved renal blood flow in hypertension have been disproved [12] Gradually, albeit reluctantly, even the surgeons have begun to admit that, despite ever more vigorously defined, but conflicting, criteria for selection of patients, few persistent cures of essential hypertension have resulted from any of the operations, and that the chief benefits of the procedures are the following a decrease in blood pressure in some patients, in others, relief of incapacitating symptoms, improvement in certain objective criteria such as the electrocardiographic or funduscopic picture, and possibly, in the case of early malignant hypertension without too severe cardiac or renal disease, a markedly significant statistical increase in survival time Peet and Isberg,[107] for example, report a five year survival rate of 21 6 per cent after splanchnicectomy in 143 cases of malignant hypertension, diagnosed on the basis of clinical course, eyegrounds, high diastolic pressure and evidences of cardiac, cerebrovascular or renal disease

Unfortunately, criteria for case selection, including the objective tests such as response to amytal, caudal or spinal anesthesia[71] and tetraethylammonium ion, have been so disappointing that often sympathectomy is attempted as the sole alternative for a desperate patient, either fearfully entering the symptomatic stage or else critically ill after trying unsuccessfully all other forms of suggested therapy Fishberg[19] presented an analysis of 119 subjects selected for sympathectomy on clinical criteria by one internist—himself, who evaluated their preoperative condition and followed their postoperative course He drew the following

conclusions Sympathectomy is only palliative and not curative despite a fall of 25 per cent or more in diastolic pressure in 25 per cent of the cases Retinopathy cleared in twelve of seventeen cases, and definite symptomatic improvement, particularly of headaches, occurred in 59 per cent, without necessarily any fall in the blood pressure Sympathectomy is indicated for patients whose future course probably will be downhill because of sudden sustained rise of diastolic pressure to 130 mm , severe retinal changes, intractable headaches, cerebral hemorrhage, hypertensive encephalopathy, or congestive failure which can respond to usual therapy, but should be suggested only after failure to respond to rigid salt restriction and bed rest It is contraindicated in patients with renal disease manifested by azotemia or hyposthenuria, in patients with systemic or cerebral arteriosclerotic symptoms, or generally in patients with congestive failure not responsive to treatment Sympathectomy is not indicated in asymptomatic patients with usual diastolic pressures of less than 130 mm Hg, and should be reserved for use later when the above indications are noted On the basis of these criteria, Fishberg concluded that this type of surgical intervention is indicated in about 4 per cent of patients with essential hypertension

Our position is about the same as Fishberg's, except that we believe that, in the confused picture which is hypertension, there must be a small percentage of patients who early in the disease may have a purely neurogenic hypertension which may be actually cured by sympathectomy Better objective means of case selection, perhaps tests with one of the newer adrenergic blocking drugs like dibenamine,[42] may some day permit us to assay the contributions of each of the several pathogenetic factors—neural, humeral or renal—in hypertension, and to uncover those patients who may be candidates for surgical cures Until then we believe that these procedures should be applied cautiously in accordance with Fishberg's indications, or experimentally in an effort to advance our understanding of the disease process in hypertension

When early evidence of congestive failure appears, the patient should be treated vigorously First complete digitalization should be achieved slowly, since there is no need for rapid digitalization, and toxic effects are less likely with the slower methods For example, administration of 0.3 gm of ordinary digitalis leaf for three days, followed by 0 2 gm once daily for two days and maintenance doses of 0 1 to 0 2 gm daily will produce digitalization in most patients The more rapidly excreted derivatives of *Digitalis lanata* (cedilanid or digoxin) may be useful, at times For cedilanid and digoxin the amounts necessary to produce digitalization administered in divided doses over twenty four hours are 7 to 8 mg and 2 0 to 3 0 mg , and the maintenance doses are 0.5 to 1 5 mg

and about 0 75 mg , respectively Because of the delay in excretion, toxic effects are more frequent and persistent with digitoxin

Secondly, gradual indoctrination of the patient in the principles of the low salt diet should be begun In early left ventricular failure, digitalization, more rest, and other changes in the patient's ordinary routine should make it unnecessary to reduce the daily sodium chloride intake to less than 4 or 5 gm , in contrast with the usual 9 or 10 gm If dyspnea, especially of the nocturnal variety, persists or recurs, mercurial diuretics should be given When mercurials become necessary more often than every month or two, the patient should be placed on the strict low salt cardiac diet which reduces the daily sodium intake to less than 1 0 gm It has been our experience that with rigid adherence to this diet fewer symptoms develop and mercurials are required much less frequently In guiding future therapy, the physician must train the patient to weigh himself daily in order to detect sudden or gradual gain in weight, which may be the first sign of occult edema

Table 2 presents sample low salt diet menus prepared by the Department of Nutrition of Montefiore Hospital Certain features of the diet should be noted Bread must be the specially prepared salt-free bread, now commercially available in some cities Those patients who prefer more than the allowed daily pint of milk, as a beverage or in cooking and baking, may use a commercial low sodium milk powder (lonalac), which may be reconstituted as desired Dairy products such as butter, of course, must be unsalted Oleomargarine and hard cheeses are not permitted because of their high salt content The following foods are permitted within the prescribed limits less than 2 or 3 tablespoonfuls of sour cream daily, no more than 3 or 4 teaspoonfuls of sweet cream for coffee or tea per meal, cottage or pot cheese if washed in cold water before using, homemade salt-free ice cream, only 2 eggs in any form daily (egg yolk contains one-fourth to one-third the sodium content of egg white but is very rich in cholesterol, a possibly objectionable feature)

Only fresh or frozen vegetables should be used, since canned vegetables usually have added salt unless specially packed Beets, celery and spinach, which contain much more sodium than other fresh vegetables, should be used sparingly or not at all All meats may be eaten except smoked, salted, canned, spiced and pickled meats, like ham, bacon, frankfurters, salami, bologna and other sausages However, lamb, mutton, or calf liver should be served no more than once or twice weekly because of their higher sodium content Fresh fish, but not shell fish or processed fish, is permitted Fresh or canned fruits, but no prepared desserts, may be served

Some patients prefer to season their foods with one of the commercial salt substitutes available, which contain either lithium chloride, citric

TABLE 2

LOW SALT CARDIAC DIET MENUS*

Breakfast	*Dinner*	*Supper*
Tangerine sections Boiled brown rice with sugar and cinnamon Poached egg on toast Butter—jelly Coffee with 2 oz. milk	Boiled beef Shredded cabbage Mashed potato Squash Stewed rhubarb Bread—jelly Tea	Chopped egg on lettuce with sliced tomato Baked potato Asparagus Canned peaches with 2 oz. cream Bread—butter—jelly Coffee with 2 oz. milk
Breakfast	*Dinner*	*Supper*
Canned apricots Shredded wheat with ½ cup milk 1 fried egg Buttered toast Jelly Coffee with 1 oz. cream	Swiss steak Braised parsnips Corn Tomato wedges Fresh blackberries Bread—jelly Tea	1 soft cooked egg Escalloped potato Green beans Fresh fruit cup Bread—butter—jelly Coffee with 1 oz. cream
Breakfast	*Dinner*	*Supper*
Orange juice Puffed rice with fruit juice 1 soft cooked egg Buttered toast Jelly Coffee with 1 oz. cream	Meat loaf Mashed potato Lettuce with lemon Frozen nectarines Bread—jelly Tea	Vegetable soup Scrambled egg Baked potato Tomato salad Watermelon Bread—butter—jelly Coffee with 1 oz. cream
Breakfast	*Dinner*	*Supper*
Pineapple juice Puffed rice with ½ cup milk Buttered toast 1 soft cooked egg Coffee with 1 oz. cream Jelly	Broiled steak Cottage fried potatoes Stewed tomatoes Corn Baked banana Bread—jelly Tea	Vegetable soup 1 sliced hard cooked egg on lettuce with tomato wedges Baked potato with butter Mixed vegetable Gelatin dessert Bread—butter—jelly Coffee with 1 oz. cream
Breakfast	*Dinner*	*Supper*
Applesauce Oatmeal with butter Scrambled egg Buttered toast Coffee with 1 oz. cream Jelly	Baked veal chop Baked potato Chopped lettuce with oil and vinegar Canned pineapple Bread—jelly Tea	Cottage cheese pudding Sour cream (small serving) Boiled potato Buttered peas Canned peaches Bread—butter—jelly Coffee with 1 oz. cream

* Prepared by the Department of Nutrition, Montefiore Hospital, New York

acid and potassium iodide (Westsal), or potassium chloride, potassium formate, ammonium chloride, calcium formate, magnesium citrate and starch (Neo-Curtasal) For heartburn or indigestion, calcium carbonate or preferably aluminum hydroxide gel is used in place of "baking soda" It should be emphasized that fluid restriction is neither required nor desirable in patients on the low salt diet In fact, some patients have no thirst and must be encouraged to drink

With frank failure, bed rest must be absolute, although bathroom privileges may be permitted Mild sedation with phenobarbital, 0 03 gm two or three times daily, is indicated, and one of the short acting hypnotics like seconal is useful at night With Cheyne-Stokes respiration, aminophylline, 0 48 gm administered intravenously, is often very effective

Coronary artery disease—anginal syndrome or myocardial infarction—in hypertensives is managed as in any other group of patients The same applies to the rarer syndrome of uremia In the management of patients with uremia it is important to watch carefully the electrolytes, and particularly sodium With the not uncommon hypertensive combination of heart failure and renal tubular failure, a delicate balance between sodium intake and output must be achieved to avoid the two opposing perils, edema from salt retention and dehydration from salt loss

Mention has already been made of unilateral nephrectomy in the treatment of hypertension Here again the therapeutic cycle has shifted from enthusiastic acceptance to critical skepticism Goldring and Chasis[12] and, more recently, Smith[34] have presented excellent critiques on the subject, from which it can be concluded that there is no evidence that there is a higher incidence of hypertension associated with urological disease, or that surgical disease of one kidney, except in very rare cases, can produce clinical hypertension in man Consequently, it is not surprising that Smith could find persistent cures of a definitely demonstrated hypertension in only 19 per cent of the 242 patients whose operations were reported It should be recalled that unsuccessful results of such operations are seldom reported Therefore, we agree with his insistence that in only a few unusually well studied cases should nephrectomy be attempted, and then not to lower blood pressure but only for established urologic indications Before operation it must be proved that the other kidney is perfectly normal or that the kidney to be removed is nearly functionless, because bilateral kidney disease is a major contraindication to nephrectomy for hypertension

In concluding this discussion of the treatment of hypertensive vascular disease, the ephemeral character of many of the purported specifics should be mentioned, if only to check the wild rumors of success which escape from the laboratory or teaching hospital by way of uncritical

newspaper or magazine articles, or unfortunately, sometimes, scientific journals For the many reasons discussed previously, the evaluation of therapy in hypertension must be based on adequate control periods and a total response of both patient and disease to the proposed specifics When subjected to such analysis, the effects of thiocyanates, nitrites, renal extracts vitamin A, vitamin K, quinones, methylene blue, tyrosinase, pituitary x-ray, etc, have been found[88 40 103] to be either negligible, nonspecific or dangerous Further advances in therapy must await a better understanding of the disease process of which elevated systemic diastolic blood pressure may frequently be the first finding[109]

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ANTICOAGULANT THERAPY IN CHRONIC CARDIOVASCULAR DISEASES

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ANTICOAGULANT therapy is the best method for preventing thrombosis and embolism which is available at present In most of the chronic vascular diseases, intravascular thrombosis plays an important role in the course and eventual outcome of the disease The complications of thromboembolism affect importantly the morbidity and to a lesser degree the mortality in many of the chronic cardiac diseases The value of anticoagulants in the treatment of, and prevention of, subsequent episodes of thrombosis and embolism is now well established The use of anticoagulants in the long term treatment of chronic vascular disease has not been extensively studied The difficulty of administration of heparin and of the control of dicumarol makes neither of these anticoagulant drugs ideal for use in large groups of cases over a period of many months or years such as would be necessary in order to estimate their value in the control of such diseases as thromboangiitis obliterans or arteriosclerosis obliterans However, the anticoagulants when properly used may play an important role in the treatment of single episodes of thrombosis and embolism and in the prevention of recurring episodes of thrombosis which may occur over a relatively short period of time (weeks or months)

The situations in which the use of anticoagulants may be advisable in chronic cardiovascular diseases are summarized in Table 1 The cardiovascular diseases and conditions in which anticoagulant therapy might be used because of the occurrence of one or several of the situations listed in Table 1 are given in Table 2

CHRONIC OCCLUSIVE ARTERIAL DISEASES

In thromboangiitis obliterans and arteriosclerosis obliterans although the primary disease involves the wall of the artery and periarterial structures, the final step causing complete occlusion is almost always due to thrombosis The occlusive episode may occur suddenly and produce recognizable symptoms of sudden arterial occlusion but most often occlusion is a gradual process of which the patient is not aware except for

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onset of intermittent claudication or coldness of the involved extremity Inasmuch as there is no way to predict when thrombosis would occur, the use of anticoagulants as a preventive would have to be continued over a long period Until more practicable anticoagulants for long-time administration are available, only in the exceptional situation should anti-

TABLE 1

SITUATIONS IN WHICH USE OF ANTICOAGULANTS MAY BE INDICATED

I	Long-term treatment of the disease (only in special situations)
II	Prevention of recurring episodes of thrombosis
III.	Treatment of single episodes of thrombosis or embolism
	A Acute arterial occlusion (including coronary artery occlusion)
	B Acute thrombophlebitis or phlebothrombosis
	C Pulmonary embolism or infarction

TABLE 2

CHRONIC CARDIOVASCULAR CONDITIONS OR DISEASES IN WHICH ANTICOAGULANT THERAPY MAY BE INDICATED

I	Occlusive arterial diseases
	A Thromboangiitis obliterans
	B Arteriosclerosis obliterans
	C Simple thrombosis
	1 Idiopathic
	2 Secondary to
	a Polycythemia vera
	b Malignancy
	c Infection
II	Venous disease
	A Primary varicose veins
	B Chronic venous insufficiency
	C Recurring idiopathic thrombophlebitis
III	Cerebral thrombosis
IV	Cardiac diseases
	A Cardiac infarction
	B Cardiac fibrillation
	C Congestive heart failure.

coagulants be used in the long-term treatment of occlusive arterial disease

Patients with thromboangiitis obliterans who are having frequently recurring episodes of thrombophlebitis may be placed on a program of dicumarol for a period of weeks or months provided that the dose of dicumarol can be regulated by determinations of the concentration of the prothrombin in the blood at frequent intervals In some instances the use of dicumarol may interrupt the "phlebitis cycle," and even after

administration of dicumarol has been discontinued, no further phlebitis will occur for a long time

It would seem that anticoagulant treatment would be ideal for the treatment of simple arterial thrombosis, a condition in which the arterial wall is normal but arterial occlusion results from a thrombosing tendency of the blood This thrombosing tendency occurs in unpredictable episodes and in this condition also the long-term use of anticoagulants is impracticable When arterial thrombosis has occurred recently or when episodes of thrombosis occur frequently, anticoagulants are of great value in preventing further episodes of arterial and venous thrombosis and pulmonary embolism If dicumarol is used, the program of treatment should be continued for several weeks or longer if possible

At the Mayo Clinic, we have given dicumarol to seventy-six patients with thromboangiitis obliterans or arteriosclerosis obliterans, in some instances for as long as four to six months In forty cases the disease was considered to be in the active phase when dicumarol was given In thirty-six it was given as a prophylactic measure after amputation In none of these cases was there any evidence of recurrence or extension of arterial or venous thrombosis during the period in which dicumarol was given

Sudden arterial occlusion is a fairly common occurrence in chronic occlusive arterial disease Such an episode always should be treated as an emergency Unless contraindicated, heparin should be given and if dicumarol cannot be used, administration of heparin should be continued for at least ten days The best type of anticoagulant treatment in sudden arterial occlusion is a combination of heparin and dicumarol The method of administration will be described subsequently

In sudden arterial occlusion, severe arterial spasm may occur not only in the main arterial trunk peripheral and proximal to the occlusion but also in many of the collateral arteries Secondary arterial thrombosis may develop as the result of damage to the endothelium in these arteries when the spasm relaxes Continued thrombosis at the site from which an embolus has been detached may be a source of other emboli When sudden arterial occlusion results from thrombosis in an artery, the thrombosis may progress proximally and produce further arterial insufficiency to the extremity The early use of measures to prevent further thrombosis is one of the cardinal principles of treatment in sudden arterial occlusion

At the Mayo Clinic we have treated eleven patients with arterial embolism in the extremities and sixteen patients with acute arterial thrombosis in the extremities with heparin and dicumarol In all of these patients the diagnosis was made early and the administration of the anticoagulants was started within twenty four hours after the embolism

or thrombosis The involved extremities of ten of the eleven patients who had arterial embolism and of thirteen of the sixteen patients who had acute arterial thrombosis were saved The results in this group would indicate that anticoagulants plus procedures to eliminate arterial spasm and avoidance of thermal trauma to the affected limb are important in the emergency treatment of sudden arterial occlusion of the extremities

CHRONIC VENOUS DISEASE

In primary varicose veins small regions of thrombosis frequently occur in varices They often result from injury to a superficial vein from striking the leg on an object, such as a chair or edge of a step Usually these regions of thrombosis remain localized and there is little or no danger of embolism In such situations, the use of anticoagulants is not necessary

When thrombosis occurs in the greater saphenous system or in the deep veins of the calf or when there is an extension of a localized region of thrombosis, anticoagulant therapy is usually advisable Anticoagulants will prevent further extension of thrombi and in the case of spontaneous thrombosis in varices will usually prevent thrombosis in other parts of the venous system and indirectly pulmonary embolism Dicumarol is the most satisfactory anticoagulant to use in such situations It should be continued for a week or ten days after subsidence of the acute thrombosis If dicumarol cannot be used because of lack of adequate laboratory facilities for determining the prothrombin activity, heparin may be given for a week or ten days

In cases of chronic venous insufficiency when the patient is to be kept in bed and relatively inactive for several weeks as part of a program for healing stasis lesions, dicumarol may be given during this time to prevent possible thrombo-embolic complications

Recurring Idiopathic Thrombophlebitis —This disease is characterized by recurring episodes of venous thrombosis over varying periods of time In some cases episodes of pulmonary embolism or thrombosis in a pulmonary vessel producing pulmonary infarctions recur from time to time Fatal pulmonary embolism is rare The most important feature is the period of prolonged disability and loss of earning power which may result from the recurring episodes of thrombosis

Anticoagulants are of value in the individual episode as this treatment when properly administered usually will prevent extension of venous thrombosis and occurrence of thrombosis in other parts of the venous system and greatly shorten the period of disability

If the episodes of thrombosis occur at wide intervals of time, such as once or twice a year, the use of anticoagulants in an attempt to prevent

further recurrence of thrombosis is not practicable When episodes occur more frequently, dicumarol may be administered for several months in an attempt to break the thrombosing cycle and to prevent frequent recurrences of thrombosis

CEREBRAL THROMBOSIS

Anticoagulants have not been used extensively in the treatment of cerebral thrombosis The extension of a cerebral thrombosis may well be prevented by the use of either heparin or dicumarol

In cases of cerebral thrombosis greater caution than usual should be exercised in keeping the prothrombin above levels at which hemorrhage is likely to occur, inasmuch as even a small hemorrhage in the brain may be disastrous We have given dicumarol to eight patients suffering from cerebral thrombosis without any hemorrhage and without any further thrombosis

The difficulty of differentiating between cerebral thrombosis and cerebral hemorrhage clinically presents a challenge to the physician contemplating the use of anticoagulants The cerebrospinal fluid should be examined to help exclude a possible cerebral hemorrhage before anticoagulants are given to a patient suspected of having cerebral thrombosis

CARDIAC DISEASE

Anticoagulants have been used in the treatment of acute coronary occlusion with cardiac infarction, in patients with auricular fibrillation and in patients with congestive heart failure The rationale for their use in coronary disease has been to prevent further coronary thrombosis and to prevent the thrombo-embolic complications often associated with acute myocardial infarction, such as venous thrombosis pulmonary embolism and thrombosis intracardiac thrombosis and subsequent embolism in cerebral and peripheral arteries The use of heparin and dicumarol for small groups of patients suffering from acute myocardial infarctions has been reported on favorably by several groups of workers

The experience at the Mayo Clinic in use of anticoagulant therapy in 100 consecutive cases of acute myocardial infarction has been reported recently by Parker and one of us (N W B) Although the mortality rate was not greatly reduced there was a striking decrease in the incidence of thrombo-embolic complications when anticoagulants were used In Table 4 the results are compared with those in a control group of similar patients not given anticoagulants reported by Nay and Barnes

Studies are now in progress under the direction of the American Heart Association to determine the value of anticoagulants in the treatment of acute myocardial infarction in 1000 patients A preliminary report on 500

cases of this group, made by Wright[10] at a recent meeting of the American Heart Association, indicated that anticoagulants will be of great value in the prevention of thrombo-embolic complications and probably in reducing the mortality rate in acute myocardial infarction

The question as to whether the use of anticoagulants might increase the incidence of myocardial rupture or of subintimal hemorrhagic lesions of the involved coronary arteries has not been settled From the data so far obtained it seems unlikely that such complications will occur much more frequently among patients treated with anticoagulants than among

TABLE 3

ACUTE MYOCARDIAL INFARCTION INCIDENCE OF VASCULAR COMPLICATIONS AFTER ANTICOAGULANT THERAPY AND IN CONTROL SERIES

	Incidence of Vascular Complications (per cent)	
	No Anticoagulant Given, Nay and Barns, 1945 (100 cases)	Anticoagulant Given, Parker and Barker, 1948 (100 cases)
Vascular complications	37	5
Second myocardial infarction	15	2
Pulmonary embolus	14	1 (2*)
Cerebrovascular occlusion	8	2
Thrombophlebitis	7	0
Peripheral arterial occlusion	4	0 (1*)

* Before admission of patient to the hospital

patients who have not been so treated Serious hemorrhage which was considered to be due to the anticoagulants used did not occur in any of the cases in the series reported by Parker and one of us (N W B)

They concluded that when laboratory facilities were available for the adequate determinations of prothrombin time, the general use of anticoagulants was justifiable for patients who had coronary thrombosis or myocardial infarction The advisability of using heparin in conjunction with dicumarol until the desired effect of dicumarol on the blood was obtained is at present debatable Inasmuch as the report of Nay and Barnes indicated that the period during which thrombo-embolic complications occur is between the fourth and twentieth days, treatment with dicumarol probably would afford adequate protection from the thrombo-

embolic complications if it was started within the first forty-eight hours of the illness Such treatment, however, would not prevent the extension of the thrombotic process in the coronary vessels or intramural thrombosis during the period of shock which often occurs early in the illness For this purpose, therefore, the early administration of heparin in addition to the starting dicumarol seems advisable Details of this program are described later

The administration of anticoagulants for myocardial infarction should be continued for at least four weeks This will give the patient protection beyond the most hazardous period, according to Nay and Barnes' series

Patients who have auricular fibrillation from any cause are subject to a relatively high incidence of thrombo-embolic complications, particularly acute arterial occlusion, because of the formation of mural thrombi in the relatively inactive auricles Patients who have chronic rheumatic mitral valvular disease are most likely to have this complication Such patients may have repeated embolic episodes with acute arterial occlusion which may result in loss of extremities or of life

When such episodes recur over relatively short periods of weeks or months, anticoagulants may be valuable as prophylactic measures against further thrombo-embolic complications Dicumarol should be used, as heparin cannot be given satisfactorily for a prolonged time To one patient with chronic rheumatic mitral disease who had had three episodes of acute arterial occlusion, we have given dicumarol for a period of two years without any further thrombo-embolic episodes

Wright[8] has under observation fifteen patients with auricular fibrillation who have had from two to twenty-one embolic episodes Dicumarol has been given for many months in these cases The longest period of observation has been sixteen months In his last report he stated that no embolism has occurred in any patient who has faithfully continued the ambulatory anticoagulant regimen The total period of freedom from embolism in the group has been more than nine years No serious complications as the result of the anticoagulant therapy have been encountered in this group

In congestive heart failure of older people, the condition of their blood vessels together with the slowing down of blood flow and lowering of blood pressure favor venous and arterial thrombosis Pulmonary embolism is a not infrequent cause of death of these patients Such patients are often kept relatively inactive for long periods of time and this inaction further favors thrombosis

In such situations anticoagulants should be of great value in preventing thrombo-embolic complication Dicumarol preferably should be given

THE ADMINISTRATION OF ANTICOAGULANTS

Heparin and dicumarol are the two anticoagulants now used clinically They should not be considered as competitors inasmuch as their different effects make them desirable as a complement to each other It is often advisable to use them together

Heparin is useful when a quick anticoagulant effect is desired and when anticoagulant treatment is to be continued for only several days or when reliable methods for determining the value for prothrombin in the blood are not available

Dicumarol is preferable when an anticoagulant effect is desired over a period of days, weeks, months or, in exceptional instances, years However, dicumarol should never be used unless reliable facilities are available for determinations of the value of prothrombin in the blood

Heparin —Heparin is effective only when given intravenously or intramuscularly At the present list price of heparin the cost for the amount of the drug needed to treat a patient adequately averages about $20 00 daily The anticoagulant effect occurs immediately when the drug is given intravenously and within a half to one hour when it is given intramuscularly

The Toronto method of continuous intravenous administration is preferable if heparin is to be given for longer than two or three days The following is a satisfactory drip method for giving heparin intravenously

Mix 200 mg of concentrated heparin in 1000 cc of either 5 per cent solution of dextrose or 0 9 per cent solution of sodium chloride Insert a steel needle ordinarily used for venipuncture into a vein on the back of the hand or arm Anchor the needle firmly and give the dilute solution continuously at a rate of 25 drops a minute Test the coagulation time of venous blood drawn from the opposite arm every four hours for the first twelve hours and every twelve hours thereafter Vary the number of drops delivered each minute so that the coagulation time remains between fifteen and twenty-five minutes If bleeding occurs, administration of heparin may be stopped and the anticoagulant effect will cease within an hour

The intermittent intravenous method is preferable if heparin is to be given for only a few days In the two methods commonly employed, heparin is administered intravenously in 50 mg doses every four hours or in 100 mg doses every six hours We prefer the first method The heparin should not be given again if excessive bleeding occurs The coagulation time will return to normal within three hours or less if this method of administration is employed This is usually quick enough to stop any persistence of serious bleeding If the action of heparin must be stopped more quickly 1 mg of protamine (salmine) given intravenously will

neutralize immediately the action of 1 mg of heparin Protamine so far is not available on the general market

In our experience the intramuscular injection of heparin in large doses (500 mg) in a slowly absorbed medium (Pitkin's menstruum) has not been *satisfactory* The deposit of the material intramuscularly often causes mild to severe pain at the site of injection The effect on the coagulation time of the blood may be variable and if bleeding occurs or there is excessive anticoagulant effect, the effect of the heparin cannot be diminished except by use of protamine which is not easily *available*, or sometimes by application of ice packs to the site of injection

Administration of heparin is not contraindicated in the presence of renal or hepatic insufficiency as is dicumarol Otherwise it is contraindicated or should be used with caution in the same conditions as those which will be listed for dicumarol

Dicumarol — After the first dose is given, the anticoagulant effect of dicumarol is delayed for from twenty-four to forty-eight hours, the delay is longer in cases in which resistance is high The effect on the prothrombin mechanism may persist for from two to five days after the last dose has been given

It is essential that the dosage of dicumarol be controlled by accurate determinations of the prothrombin time (Quick method) daily for the first three or four weeks and not less than once a week thereafter if treatment is to be continued

Some important features of the *Quick test of prothrombin time* are as follows

Thromboplastin used in the Quick method when *prepared from different sources* and by *different technics* may vary *considerably* Therefore, it is necessary to standardize the test whenever a *new* batch of thromboplastin is used

Whenever a new supply of thromboplastin is *obtained*, even if from the same source as that previously *used*, the following *control data* should be obtained on three normal individuals (1) the average prothrombin time in seconds of undiluted *plasma* this may be designated as T^{100} (2) the average prothrombin time in seconds of 30 per cent plasma in 0 9 per cent solution of sodium chloride which may be designated as T^{30} (3) the average prothrombin time of 20 per cent plasma in 0 9 per cent solution of sodium *chloride* which may be designated as T^{20} and (4) the average prothrombin time of 10 per cent plasma in 0 9 per cent solution of sodium chloride which may be designated as T^{10}

If these designations of prothrombin time are adhered to, there should be little confusion in regulating the dosage of dicumarol given the patient as far as the interpretation of the results of the test is concerned

The dosage of dicumarol should be so regulated that the prothrombin time is kept as near as possible between that known at T^{30} and that known as T^{10}

A satisfactory program of dosage of dicumarol is as follows

1 Give entire amount for one day in a single dose by mouth

2 Give 300 mg as the first dose

3 Give 100 mg on each subsequent day that prothrombin time is shorter than T^{20}

4 Give no dicumarol on days when prothrombin time is longer than T^{20}

5 If patient is resistant to dicumarol, increase dose from 100 to 200 mg on each day that the prothrombin time is shorter than T^{20}

6 If prothrombin time is longer than T^{10} for two successive days, give 36 mg of menadione bisulfite (synthetic vitamin K) intravenously

Major bleeding from the effects of dicumarol is unlikely if the prothrombin time does not fall below T^{10} If minor bleeding occurs, no more dicumarol should be given until the possibility of major bleeding and the urgency of the need for anticoagulant therapy is evaluated

If major bleeding occurs, no further dicumarol should be given Seventy-two milligrams of menadione bisulfite (synthetic vitamin K) should be given every eight hours until the bleeding stops A transfusion of fresh citrated blood should be given and repeated as often as necessary and as long as there is evidence of serious deficiency in the blood If the dosage of dicumarol is carefully regulated according to the afore-mentioned program, serious bleeding may be anticipated in less than 1 per cent of patients receiving dicumarol

Dicumarol should not be used in the following situations (1) in the presence of renal insufficiency, (2) in the presence of hepatic insufficiency, (3) in cases of purpura of any type, (4) in cases of blood dyscrasia with bleeding tendency, (5) in cases of subacute bacterial endocarditis, and (6) after operations on brain or spinal cord

Dicumarol should be used cautiously if at all in these situations (1) when there is an active peptic ulcer, (2) when there are open granulating wounds, other ulcerations or potentially bleeding surfaces, (3) when there are drainage tubes in body orifices or surgical wounds, and (4) when there is severe dietary or vitamin deficiency

Combined Administration of Heparin and Dicumarol.—When an immediate effect from an anticoagulant is desired and when anticoagulant therapy is to be continued for several days, the combined administration of heparin and dicumarol is the best method The procedure is as follows Give dicumarol according to the program already outlined Give heparin intravenously in doses of 50 mg every four hours Determine the prothrombin time daily The blood for the prothrombin test should be drawn

at least three and a half hours after a dose of heparin has been given, otherwise the heparin may alter the results of the prothrombin test The administration of heparin should be discontinued when the prothrombin time is longer than T[illegible]

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PHYSICAL MEDICINE IN PERIPHERAL VASCULAR DISEASES

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THE role of physical medicine in peripheral vascular diseases extends into the fields of diagnosis, of treatment of the disease and of rehabilitation of the patient

PHYSICAL DIAGNOSIS

The diagnosis of peripheral vascular diseases is usually fully discussed in general reviews Here it will be treated briefly One cannot consider physical diagnosis itself part of physical medicine Specific physical measures are useful mainly in arterial disease to establish the presence of arterial spasm or excess vasoconstrictor tone and to evaluate the extent of collateral circulation These are important diagnostic questions, decisive for prognosis and directing the therapeutic approach The following physical procedures are of proven diagnostic value and are easily applied

Landis-Gibbon Test —The principle of the Landis Gibbon test[1] is to produce vasodilatation reflexly by application of heat to a skin area distant from and not involved in the vascular process For example, in disease of the lower extremities heat is applied to the upper extremities The stimulation of heat sensitive nerve endings in the skin and the increase in the temperature of the blood produces through the hypothalamic temperature centers a release of sympathetic vasoconstrictor tone in the lower extremities This increases the temperature of the toes to or near to the possible maximum, normally 92° to 94° F The test is carried out as follows The patient immerses both forearms and hands in water of 110° F He is well covered with blankets up to the neck except for the feet which are lightly covered with a towel His mouth temperature is taken at the beginning and at fifteen minute intervals and should rise 1° to 2° F within one half hour The toe temperature will usually reach a maximum after thirty minutes, rarely sooner or after forty five minutes The skin temperature can be measured with a thermometer or guessed fairly well by simple palpation

Heating pads or diathermy electrodes on upper extremities or on the trunk may be substituted for the above procedure The effectiveness of the test is then gauged by the elevation of mouth temperature

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In a study of upper extremities heat is applied to the lower limbs

The Landis-Gibbon test produces a rise of toe or finger temperature to the normal 92° to 94° F independent of the initial skin temperature, at the usual room temperatures It results in a normal maximum rise if the circulatory disturbance is vascular spasm or increased vasoconstrictor tone In cases of organic arterial obstruction the degree of temperature elevation depends upon the extent of collateral circulation in the skin and the extent of complicating superimposed vascular spasm If a patient with obliterating arteriosclerosis or thromboangiitis obliterans obtains an elevation to 88° F from an initial 75° F his circulatory reserve must be better than if the toe temperature rises in another case to 80° F Prognosis is therefore better in the first instance even if foot and popliteal pulses are equally absent and oscillometric readings equally low in both cases

The result of the Landis-Gibbon test depends upon an intact reflex arc In severe peripheral neuropathy or in central nervous system disease interrupting the reflex, the test may fail In rare instances a normal person may show an incomplete vasodilatation Perspiration will depress skin temperature but does as a rule occur proximally to the digits

Reactive Hyperemia Test.—Independent of innervation is the reactive hyperemia test devised by Lewis and Pickering[1] Tissue anoxia is followed by vasodilatation and hyperemia after restoration of circulation The rapidity and intensity with which hyperemia appears is a measure of circulatory reserve The patient rests in a warm room If necessary the involved extremity is first warmed for ten minutes in water of 97° F to abolish vasoconstriction The limb is then elevated above the heart level to drain blood out and a blood pressure cuff around the lower thigh is inflated to above systolic pressure, e g , to 200 mm of mercury Pressure is maintained for five to ten minutes and then suddenly released A bright red and intensive hyperemia appears normally on the digits within a few seconds A normal result may also be expected in patients with vasospasm In organic arterial obstruction hyperemia is delayed up to several minutes and is faint or of a dusky purplish hue according to the severity of involvement

Test for Raynaud's Syndrome.—In Raynaud's syndrome and related instances of *digital arterial spasm* upon exposure to cold, the hands or feet are usually immersed in water of 55° F for five to ten minutes to reproduce an attack Sometimes, however, it is necessary to use ice water for one or several minutes—a combination of cold and pain stimulus Rarely, but especially in the summer, cooling of the whole body with a cold shower is required In the normal person, cold produces vasoconstriction which is followed by hyperemia after, and often during, exposure The patient with Raynaud's syndrome reacts with an intensive

vascular spasm The digits appear waxy or bluish for many minutes and there is not always a subsequent period of reactive hyperemia

Ergometry —While we are fairly well equipped to estimate blood flow in the skin, the *circulation of muscle* cannot be measured with clinical methods Various ergometers have been used for a quantitative approach to the problems of intermittent claudication These instruments do not eliminate the subjective factors involved in fatigue and pain and are not more exact than simple walking tests

Diagnosis in peripheral vascular disease requires many more observations These are not within the limits of the present discussion A complete diagnosis must attempt to establish (1) the type of vascular disease, (2) the level of involvement, (3) the presence of vascular spasm and vasoconstriction and (4) the extent of circulatory reserve *Only on the basis of a detailed diagnosis can a rational approach to treatment be made*

TREATMENT

Physical agents play a major role in the therapy of chronic arterial diseases The blood flow to a limb or parts of it is temporarily or permanently diminished as a result of arterial spasm (e g , in Raynaud's syndrome) or by organic vascular occlusion as in thromboangiitis obliterans and arteriosclerosis obliterans Frequently there is a combination of organic obstruction and vascular spasm If the blood flow is insufficient for the requirements of the tissue, anoxia manifests itself in intermittent claudication, rest pain and trophic changes The *imbalance between metabolic needs and blood supply can obviously be corrected by reducing the first and increasing the la ter*

CASES SHOWING SOME CIRCULATORY RESERVE AND WITHOUT PROGRESSIVE GANGRENE OR INFECTION

If diagnostic tests show some degree of circulatory reserve *and in the* absence of progressive gangrene or infection, the therapeutic problem is to *improve the blood flow* The means are *vasodilatation, release of vaso spasm* and of *sympathetic vasoconstrictor tone* If possible a simultaneous increase in metabolism is avoided Maintaining or *repeatedly* inducing vasodilatation apparently favors the *development* of collateral circulation Physical medicine offers three *ways of* increasing the circulation of a limb (1) application of heat, (2) local introduction of chemical vasodilators by physical *means* and (3) mechanical alteration of blood flow

Heat Heat *applied* locally produces *active hyperemia* with an increase of blood flow of several hundred *per cent* It *increases* local tissue temperature and *metabolism and thereby* the requirement for blood In severe arterial obstructive disease the increase in metabolism is fa

quently greater than the possible increase in blood flow The result is more tissue anoxia and a serious danger of burns Heat is the physiologic stimulus for vasodilatation in the skin Contraction is the physiologic stimulus for vasodilatation in muscle

Heat may be used in three forms

1 *Superficial heat* is produced by radiation from a baking lamp or by conduction from a heating pad or a hot bath Penetration is about 1 inch (by conduction) Vasodilatation occurs locally, possibly by release of histamine, and reflexly In vascular disease these heat applications should be mild and of rather long duration, e g , a foot bath with a temperature of 100° F for thirty minutes two or three times daily A baking lamp with a 250 watt bulb can be used from a distance of 3 feet for about twenty minutes Infra-red elements are applied in the same way and offer no advantage over luminous heat Indications are vasospasm, increased vasoconstrictor tone and mild obstructive arterial disease with good circulatory reserve If the patient complains of increased pain during or after treatment it should immediately be discontinued Heat is *contraindicated* in advanced cases of chronic arterial disease and in arterial embolism, especially in the presence of sensory disturbances If doubt exists concerning the severity of the circulatory impairment, heat should be used at first only under direct medical supervision

Luminous heat may also be used continually under thermostatic control at air temperatures of 95° to 97° F (with a bulb and the thermostat in a cradle) This is permissible in all except the very severe cases of organic disease It is not advisable in arterial embolism

2 *Penetrating heat* is produced by diathermy and short wave diathermy apparatus [2] Conventional diathermy is impractical except in hospitals The amount of heat generated by short wave diathermy in muscle or other deep tissues and the corresponding vascular dilatation cannot be measured Heat is not the physiologic stimulus for vasodilatation in muscle The danger of overheating and burns is much greater with diathermy than with superficial heat Diathermy burns heal especially poorly Direct diathermy heating is permissible in spastic or mainly spastic arterial disease These vasospastic disorders manifest themselves chiefly in the digits and the skin where superficial heat is quite effective *There is little use for direct short wave applications in the treatment of vascular disease*, especially in general practice

3 The most useful form of heat therapy in peripheral vascular disease is *reflex heat* [3, 4] Its principle is discussed above (Landis-Gibbon test) It will raise tissue temperature and metabolism only as far as blood flow and blood temperature increase in the involved limbs There are various technics of application The Landis-Gibbon procedure itself may be used for therapeutic purposes More conveniently, one or two heating pads

are applied on the patient's lower back and abdomen. The patient should be well covered with blankets, especially his legs. The treatment may last one hour and be given daily. It can be made more effective by taking hot fluids. Similar results will be obtained by application of short wave diathermy on the trunk or on the uninvolved upper extremities.

Reflex heat is in fact a mild form of hyperthermia (fever) treatment. It should be used only if the Landis-Gibbon test shows an elevation of skin temperature in the involved area. It increases mainly the blood supply of the skin, not of the muscle. Indications for reflex heat are the severer cases of organic arterial obstructions, and arterial embolism. *Reflex heat is a safe and effective means of producing vasodilatation.* Fever therapy—in fever cabinets or by typhoid injections—has probably no advantage over reflex heat in peripheral vascular disease.

A measure which is still sometimes recommended is *alternate baths.* The involved extremity is immersed in moderately cold and warm water for varying periods of time. This represents supposedly vascular exercise. However, in vasospastic and in organic arterial disease it is desired to produce vasodilatation and collateral circulation. Cold applications are rarely advisable. The disadvantages of direct heat applications have been discussed. *There seems to be no justification for an alternate use of heat and cold.*

In conclusion, one can say that *heat is one of the most effective physical means of producing vasodilatation, especially in the skin.* Direct heat applications are indicated in vasospastic conditions and mild cases of chronic arterial obstructive disease with satisfactory circulatory reserve. In most instances superficial heat is effective and less dangerous than penetrating heat. *In severe cases of organic arterial disease reflex heat should be used if effective.* Direct heating should be avoided. Heat applications in chronic vascular disease must as a rule be extended and repeated daily over periods of several months before beneficial clinical results become obvious.

Vasodilator Drugs. The use of vasodilator drugs is common in peripheral vascular disease. Their number is relatively great and their actions are still being studied. If they are given by oral and parenteral routes a great deal of their effect appears in areas where the circulation is adequate. Two vasodilator substances can be introduced directly into the skin of the involved limb by means of a galvanic current. This procedure is called *ion transfer, iontophoresis* or *electrophoresis.* It is used with histamine or with mecholyl salts. * * *Histamine and mecholyl* are positive ions and migrate with a galvanic current from the positive pole towards the negative. *Applied* on the skin they produce an intensive hyperemia and histamine also causes wheal formation. The increased blood flow lasts from one to several hours. Although the m

solutes by electrophoresis is limited to the epithelial layers, hair follicles and coil glands of the skin, a reflex spread of hyperemia occurs to deeper tissues as well as to adjacent skin areas Histamine and mecholyl electrophoresis may be used in all cases of organic or spastic arterial disease if these vasodilators show a positive response upon intradermal test reactions It also is applied on the skin around ulcers to improve their blood supply It may be given daily or several times weekly over periods of several months *This treatment appears to be of definite value for the development of collateral circulation*

Histamine is usually applied in solution of 1 3000 or 1 5000 of the biphosphate, with a current of 0 25 milliampere or less per 1 sq cm of surface for ten to fifteen minutes Mecholyl is used in a 0 25 to 0 5 per cent solution for fifteen to thirty minutes with the same current strength Asbestos paper is saturated in these solutions, snugly applied to the skin and by means of copper mesh electrodes connected to the positive pole of a galvanic generator Both substances may also be used in the form of an ointment, Imadyl Unction and A B M C ointment respectively, which is rubbed into the skin The area is then covered with a thick cotton pad soaked in saline to which the positive electrode is attached Electric burns can be entirely avoided with this last method Systemic reactions with histamine are rare and subside with the patient at rest in the supine position Mecholyl reactions can be counteracted with atropine (1/100 grain subcutaneously or intravenously)

While effective amounts of these two vasodilators can be introduced into skin only by electrophoresis, *carbon dioxide will migrate from a solution according to pressure gradients* into and through the skin Carbon dioxide is a powerful dilator of peripheral blood vessels [7] Its effect does not spread reflexly and disappears within a short time Carbon dioxide baths can be used to produce vasodilatation in the skin in vasospastic and organic arterial disease Such a bath can easily be prepared in the patient's home In a wooden barrel or any nonmetallic container of suitable size, ¼ pound of baking soda is dissolved in each 2 gallons of water The water temperature may be between 90° and 95°F The patient immerses his feet and legs For each ¼ pound of bicarbonate of soda 100 cc of commercial hydrochloric acid, previously diluted with 300 cc of water, is slowly introduced through a clamped rubber tube to the bottom of the container A stream of fine gas bubbles should appear The duration of the bath is fifteen to thirty minutes It may be given daily Ulcers or gangrene are a contraindication

The local introduction of vasodilator substances by physical means is mainly indicated in the *advanced stages of arterial disease* where direct heat is not advisable and reflex heat is ineffective It permits the application of the vasodilator to the diseased area while vasodilators by the oral

or parenteral route have a systemic effect. Its action is however primarily and mainly upon skin circulation. The effects of histamine or mecholyl electrophoresis are more intensive and last longer than those of carbon dioxide bath. Carbon dioxide, however, is an effective vasodilator even in cases in which the former substances fail. Frequently the vascular response to these substances increases during a course of treatments. Their therapeutic value for the development of collateral circulation and for the healing of indolent ulcers appears well established.

Mechanical Measures.—Mechanical measures have been a stand-by in the treatment of vascular diseases for many years. Generally these measures intend to increase arterial inflow and favor the venous return by increasing and decreasing the hydrostatic pressure within the blood vessels of a limb.

The oldest and simplest of these procedures is *Buerger's exercise*. The legs of the supine patient are elevated and rested on a support (with an angle of 30 to 60 degrees) until blanching appears (1 to 3 minutes). Then the legs of the lying or sitting patient are lowered to a hanging position until they show rubor. This is followed by a rest period in the horizontal position of five minutes during which a heating pad is applied to the feet. Such exercises are carried out one or two times daily for half an hour.

The use of a heating pad in severe cases of arterial obstruction is objectionable. It appears doubtful whether changes in hydrostatic pressure will overcome vascular spasm and open up collaterals. The main effect is probably to drain and engorge subpapillary venous plexuses and capillaries of the skin.

Changes in hydrostatic pressure without effort of the patient and continuously through the day are produced in the *oscillating bed*.[8] It appears to have a pain relieving effect in vascular disease. Its influence upon the blood flow has not been thoroughly studied as yet.

Highly esteemed in the treatment of chronic arterial disease and arterial embolism about ten years ago was the *pneumatic boot*.[9] The diseased extremity is fitted with sponge rubber into a boot in which negative pressures of 60 to 80 mm. of mercury for three to four minutes are produced alternately with positive pressures of 20 to 30 mm. of mercury for one to two minutes. During the period of negative pressure the arterial inflow is enhanced, during the positive pressure the venous outflow. There are experimental and theoretical objections to such simple assumptions. Clinical observations have made the value of the pneumatic treatment more and more doubtful and in recent years it has rarely been used. It is contraindicated in presence of infections, ulcers or gangrene.

In intermittent venous occlusion[10] a blood pressure cuff attached to the

involved extremity, e g , on the thigh, is automatically inflated to pressures of 30 to 90 mm of mercury After one or several minutes the pressure is released for periods of a minute or more This treatment is maintained for hours or the greater part of the day No definite rules are available by which to regulate the pressure or the timing During the period of pressure, venous congestion occurs which may facilitate the utilization of oxygen in the tissues During the interval, reactive hyperemia appears if a pressure of 40 mm or more of mercury is applied Most clinical observers agree that intermittent venous occlusion does not increase collateral circulation It does not improve intermittent claudication or rest pain and does not change the course of localized gangrene or the fate of an extending necrotic process It is of value for the healing of indolent chronic ulcers in arterial occlusive disease The safest means of application is to start with a 30 to 40 mm pressure, two minutes on and two or three minutes off, for one to two hours If tolerated without pain the pressure may be increased to 50 to 60 mm for two to three minutes and the treatment continued for six to twelve hours daily

The most powerful and the simplest measure to produce vasodilatation in muscle is *exercise*, e g , walking Contraction is the physiologic stimulus for hyperemia in muscle The hyperemia is produced mainly by local release of vasodilator metabolites affecting the small blood vessels Obviously, muscle contraction increases the tissue metabolism and its requirements for blood The discrepancy between demand and supply of blood in contracting muscle and the resulting ischemia is responsible for the pain of intermittent claudication If ischemia in walking is limited to mild degrees of brief duration there is no danger of irreversible tissue changes Walking is the most effective means of vasodilatation and of increasing circulatory reserve in muscle *In the presence of gangrene, of ulcers, of rest pain or of ischemic neuritis, walking is as a rule contraindicated In all other cases of peripheral arterial disease walking should be prescribed as a therapeutic measure* The patient walks at a slow pace until the first pain appears, then rests standing still or sitting until it subsides, and repeats this for a total of about thirty minutes, twice daily Some patients observe that their walking capacity increases after the first or second rest period In others, however, walking distance diminishes during exercise, probably because they develop additional arterial spasm In the latter case the patient should rest before pain occurs

Massage of the involved limb is another means of producing vasodilatation in muscle and skin It increases venous return and lymph flow According to present knowledge, massage does not increase the metabolism of tissue Its effects actually need thorough investigation Massage may be used as stroking (effleurage) of muscles daily for fifteen

minutes combined with resistive exercises in suitable cases Massage is contraindicated in the presence of infection, thrombophlebitis, varicosities and larger ulcers or gangrene

These are the more important physical procedures to improve circulatory reserve and abolish vascular spasm in arterial disease In most instances one will combine several measures to dilate skin and muscle vessels, e g, reflex heat and walking exercises or histamine electrophoresis and walking exercises Usually *vasodilator drugs* are also prescribed It is impossible to evaluate under these circumstances the therapeutic effect of the single procedure This is the reason why *opinions* vary considerably In the previous pages the clinical impressions of the present author are reported A reliable statistical or controlled integration of these personal experiences and the published material does not appear possible

Ulcers in arterial disease present the problem of wound healing in addition to circulatory difficulties *Ultraviolet radiation* appears sometimes to stimulate wound healing If the surrounding skin is covered, the ulcer may be exposed to several erythema doses every other day It is useless to apply ultraviolet radiation to a slough-covered surface

Advanced Cases of Arterial Disease

In advanced cases of arterial disease without a noticeable circulatory reserve, in the presence of continuous ischemic pain, and in cases of extensive and progressive gangrene or ulceration, *attempts at vasodilatation* are useless and in rare instances even dangerous The only way of *reducing ischemia is to diminish the local metabolism* This can be done by *rest* and by the local use of *cold* The disadvantages of complete physical inactivity are well appreciated at the present time However, patients with gangrene, larger ulcers or infections must be kept off their feet They should rest with the involved limb in the horizontal position If gangrene is extending or markedly infected or if osteomyelitis is present, even bathroom privileges should be denied

Refrigeration[11] in peripheral vascular disease is medical or anesthetic (preparatory to amputation) Only the *first will be discussed* here Refrigeration undoubtedly lowers tissue metabolism and requirements for blood It also *produces vasoconstriction by a direct* action upon the blood vessel and by reflex action The reflex effect spreads throughout the surface of the body It is not known whether the diminution in metabolism balances or outweighs the decrease in blood flow, either in the normal person or in one with vascular disease It is also not known how the circulation of the muscle reacts to cooling However, clinical experience shows that in some cases severe ischemic pain, in others the rapid progress of gangrene or infection may be easier controlled with the

additional aid of refrigeration In rare instances a limb can be saved and active treatment of the vascular lesion attempted after refrigeration has lessened the impact of the circulatory catastrophe over a period of several days In such patients repeated paravertebral blocks may minimize the reflex constrictor effects of cold In the majority of cases refrigeration is a means of postponing amputation, e g , for the purpose of improving the general condition This is true in chronic arterial disease and in cases of arterial embolism

Medical refrigeration may be applied with special apparatus A skin temperature of 65°F is desirable Cooling is maintained for four to six hours and then interrupted for one to two hours while the patient and his limb reactions are observed Four ice bags will serve about as well for a leg The extremity is well covered with towels or sheet cotton and a rubber sheet Another rubber sheet is placed on the bed The ice bags are arranged on both sides of the leg No pressure on the leg and no wetting should be permitted Timing of the application is as above Refrigeration may be maintained for a few days, a week, or even longer

REHABILITATION

Rehabilitation is the planning and facilitation of the adjustments which a patient has to make for his return to self-dependency and economic usefulness if his disease is chronic or left him with a physical defect *The program must begin while the patient is under active treatment* for his disease It consists in patients with peripheral vascular diseases of the following phases (1) Preventive measures against disabling deformities and atrophy of muscles and bone not directly due to the vascular lesion, (2) early preparatory training for and later actual resumption of physical activity, (3) supply with proper mechanical appliances and instruction in their use if necessary, (4) vocational guidance and training, (5) psychological readjustment of the patient Although these phases form an inseparable unit, only a few points can be mentioned here

Preventive Measures.—Patients with painful lesions on their feet at bed rest develop *flexion contractures of the knees,* sometimes with great rapidity, within two to three weeks It is a terrible experience to find a knee in 120 degree flexion and the patient unable to walk after treating a superficial gangrene of the large toe successfully A flexion contracture of the knee may necessitate a midthigh amputation (mortality 25 to 30 per cent) when the vascular lesion itself is suitable for a local amputation (negligible mortality) Little can be done once the contracture is established In the presence of poor circulation, traction and other

orthopedic measures are badly tolerated It is easy to avoid the contracture if the patient is forced to stretch the knee actively or passively and keep it fully extended for about ten minutes every hour Needless to say that in the bedridden patient with vascular disease the heel is protected from pressure by proper padding The foot should be kept under a cradle to avoid the pressure of the covers which favors the development of a foot drop

Early Preparatory Training —*Active use of noninvolved extremities* for the purpose of self-care is immediately instituted in every bedridden or chair-ridden patient If a prolonged period of bed care is expected, daily resistive exercises and massage for the intact extremities and a schedule of light exercise for the diseased extremity are added Occupational exercises are important for the maintenance of motor functions and morale and can be improvised anywhere without much expense and difficulty

Mechanical Appliances.—No discussion is required of the importance of proper selection of crutches, canes and prosthesis in the case of amputees Most amputees adjust themselves to a preliminary crutch gait rapidly without a prosthesis They walk later with *one cane on a midthigh prosthesis* and without a cane on a midleg prosthesis Much attention is needed for the correction of *foot deformities* which develop without or following minor surgical procedures If the body weight is thrown excessively upon the metatarsal heads, poorly padded by atrophic subcutaneous fat tissue and skin, walking becomes unbearably painful Metatarsal bars and heels may be insufficient and rubber cork insoles are required which are carefully shaped to relieve pressure on bony protuberances

Vocational Guidance Psychological Readjustment —The questions of vocational guidance and the psychological problems of the patient with peripheral vascular disease cannot be more than mentioned here It must suffice to say that occupations with exposure to cold or with the need for stair climbing or strenuous fast walking are unsuitable The majority of patients with thromboangiitis obliterans and probably all with Raynaud's syndrome are emotionally unstable, over reactive and unable to cope with routine problems of life They respond with vasoconstriction and alarm reactions very readily The popularization of ischemic and publicity have succeeded in putting enough fear of hardening of arteries and of Buerger's disease into people to make them manifestly neurotic or hypochondriac if confronted with these diagnoses Psychologic or even psychiatric help is an essential part of their rehabilitation Care in communicating the diagnosis is of great importance

SUMMARY AND CONCLUSIONS

Peripheral arterial diseases are typical diseases for long-term care and rehabilitation There are no cures and no satisfactory means to restore circulation within a brief period of time Sympathectomy is of limited value or frequently disappointing If, however, medical measures and suitable physical agents are applied over periods of many months and are combined with good general and local care, a good many of these patients can be improved enough to enjoy their lives and be useful to their families and the community Moreover, active treatment should commence before irreversible trophic changes are established This is especially important for the amputee whose remaining limb usually shows an impaired circulation It deserves immediate attention

An attempt was made in the preceding pages to present critically the role of physical medicine in the diagnosis and treatment of peripheral vascular disease and in the rehabilitation of the patient The scientific basis, the clinical value and the technics of methods were briefly discussed if these methods were considered useful or important in medical practice

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TREATMENT OF HEART FAILURE

SOL BILOON, M D *

At the beginning of this century the average duration of life was fifty years, today it is between sixty-five and seventy years With the control of infectious diseases an aging population has been produced As people become older, they require more medical care, so that today the care of chronic illness is the main concern of the doctor, the family, the hospital and society The most important chronic, long-term illness is heart disease

More than half of all patients with heart disease will have heart failure during their lifetime With the first evidence of heart failure treatment should be planned on a long-term basis Most patients can be helped to lead useful lives in the presence of heart failure, *often for many* years Recent investigation into the nature and mechanism of heart failure has provided new knowledge which is *being utilized* to make treatment more effective Patients with heart failure can be made much more comfortable, the period of hospital care can be shortened, and many more patients can be restored *to useful activity*

Certain general principles of treatment for long term illness apply with special force to the treatment of heart failure It is essential to help the patient adjust to an illness that he fears He must accept necessary restrictions in activity and diet He must be taught the importance of rest, but no unreasonable *or petty privations* should be enforced *The patient must be encouraged* by the knowledge that newer *methods of* treatment offer much hope of increased life expectancy and useful living The doctor needs to cultivate a hopeful attitude and should try to transmit this *attitude to the* patient Fear must be avoided, since an anxiety state with *reference* to the heart is often more resistant to treatment than the *underlying heart* disease itself

NATURE OF HEART FAILURE

The modern knowledge *of heart failure* is based on the physiological experiments of Starling on the isolated mammalian heart and confirmed by others for the intact *mammalian heart* Starling found that the main factor which determines the output *of the heart is the* pressure in the right auricle and its tributary veins With a rise in pressure in the right auricle there is increased diastolic filling of the ventricle with an increase

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in the volume of blood in the ventricle and an increase in the length of the heart muscle fibers These changes increase the energy of systolic contractions and produce a greater cardiac output It will be seen from *Figure 137 that a rise in venous pressure provides a rise in cardiac output* until a point is reached near the peak of the curve where the increment in cardiac output begins to diminish with each subsequent rise in venous pressure When the peak of the curve is reached there will be no increase in output with an increase in venous pressure This means that the re-

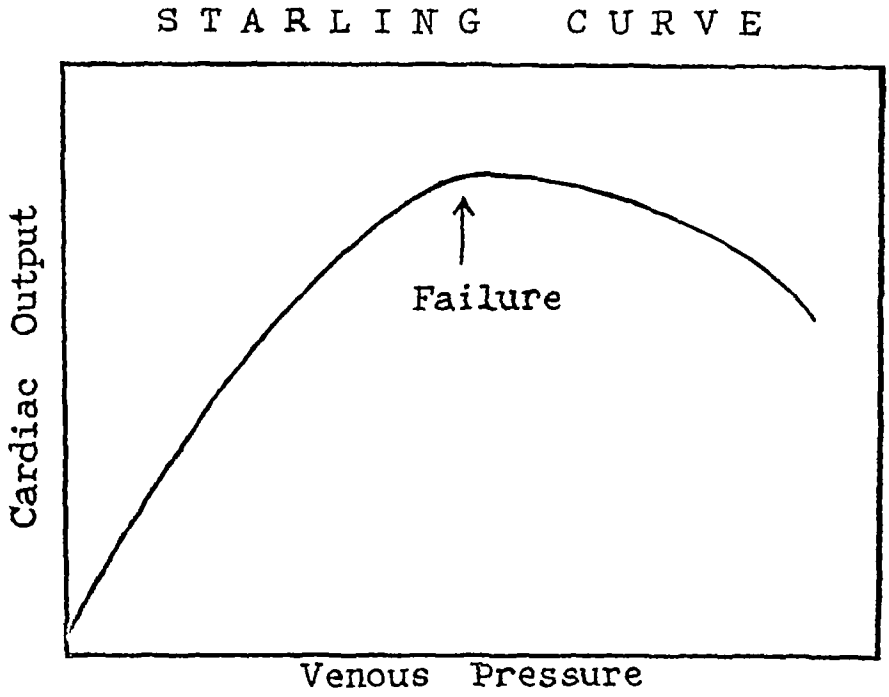

Fig 137 —Cardiac output in relation to venous pressure

serve power of the heart begins to grow less after a time When the peak of the curve is reached a further increase in venous pressure causes a drop in cardiac output and evidences of failure appear

Other factors also influence the cardiac output The rate of the heart is increased by some extracardiac factor when there is a rise in venous pressure This may serve to increase the output of the heart per minute However, excessive rates which do not allow time for adequate diastolic filling of the ventricles may cause the heart to fail Small amounts of adrenalin raise the cardiac output without any rise in venous pressure or increase in heart rate [10]

The failing heart responds to a rise or fall in venous pressure by a rise or fall in output, depending on whether its functional state places it on the rise, the peak or the decline of the Starling curve

The normal heart rarely fails It is usually able to meet any increased venous return by increased output As an example of the mechanism by which the normal heart meets an increased demand, the bodily changes which take place in exercise may be reviewed

1 Increase in blood flow through muscles
2 Mobilization of blood from blood depots
3 Increase in circulatory blood volume
4 Increased venous return to the heart
5 Increased heart rate
6 Decreased renal blood flow

The above pattern of response to increased metabolic demand through the reflex and hormonal control of venous pressure, heart rate and renal blood flow is the same pattern which is observed when the heart fails and the output of the heart must be raised to meet metabolic demands The normal cardiac output in young subjects is 4 to 8 liters per minute In older subjects the pulse rate is more steady and the output is closer to 5 liters per minute When the heart muscle has been damaged by disease as in rheumatic fever or coronary disease or when it has been subjected to an increased mechanical load as in hypertension, the time comes when the various factors which serve to increase cardiac output are no longer able to provide a circulation necessary to meet even normal demands At this point the cardiac output falls and the symptoms and signs of heart failure appear This is the most common type of heart failure seen in clinical practice, sometimes called *low output failure*

Less frequent, but of great theoretical importance, is the type of heart failure which appears in patients in whom there is little damage to the heart muscle by disease but in whom there is a great demand for increased work by the heart under conditions which gradually reduce the efficiency and strength of contraction of the heart muscle This type of heart failure is seen in anemia hyperthyroidism, cor pulmonale and arteriovenous shunts In these patients the need for oxygen and other metabolites is so great that the heart responds by the usual mechanisms and increases its output above the normal Despite this increase such a heart after some time fails to provide an adequate circulation This type of heart failure is called *high output failure* It is probable that although the cardiac output in such patients is higher than normal it is not high enough to meet the extraordinary metabolic needs[1]

The heart also fails when its chambers cannot be adequately filled because of excessive heart rate or constrictive pericarditis When the mechanism for increasing diastolic filling breaks down,[1] as in shock the heart will also fail In these conditions a reduction in cardiac output occurs

The exact sequence of the events which take place in heart failure

is not clear and no satisfactory concept which will explain all the observed facts is available [3] I believe that the cause of the symptoms and signs of heart failure is to be found in the changes which take place in the body when the cardiac output is not sufficient to meet metabolic demands In order to increase diastolic filling pressure and cardiac output, there is an increase in blood volume and venous pressure and a decrease in renal blood flow From these changes the major clinical phenomena of heart failure have their origin

ORIGIN OF MAJOR SIGNS OF HEART FAILURE

Dyspnea Increased venous pressure in lungs, encroachment of engorged veins on air space, less air in lungs, less oxygen in arterial blood Because of engorged veins and edema of alveolar walls, the lungs are less elastic and more rigid Vital capacity is reduced

Orthopnea Shift of pooled blood from extremities to lungs in recumbency with increased blood volume and increased venous return to lungs Increased venous pressure at respiratory center

Edema Reduction in renal blood flow with decrease in rate of filtration of sodium Normal resorption of sodium by the tubules Sodium and water retained by the body Increased blood volume and venous congestion and edema result [8 12 13 16]

Cyanosis Increased venous pressure in lungs produces congestion with inadequate aeration of blood in lungs Another factor may be the extraction of more oxygen from the tissues, owing to increased tissue requirements

It will be seen from the foregoing that the mechanisms of the body which operate to raise the output of the heart to the required level are responsible for the clinical picture of heart failure

CAUSES OF HEART FAILURE

Causes of heart failure in diseased hearts include

1 Gradual diminution in cardiac reserve due to excessive load as in hypertension or to mechanical defects as in rheumatic heart disease This is the most common variety of heart failure which I see It comes on gradually, occurring when the functional capacity of the heart is such that it can no longer meet the metabolic needs of the body without an increase in venous pressure and a decrease in renal blood flow These in turn bring about the signs of congestion of the lungs and edema

2 Infections Rheumatic infection is the most frequent cause of heart failure in children Other common infections, especially respiratory infections, may cause heart failure

3 Sudden excessive exertion and overeating

4 Paroxysmal rapid heart action

In normal hearts, heart failure may occur as a consequence of hyperthyroidism, chronic pulmonary disease and severe anemia This type of heart failure is caused by an excessive metabolic demand which is not satisfied despite the best efforts of the heart muscle to meet it In these patients the cardiac output may be raised to twice or three times the normal value and failure may appear In hyperthyroidism the basal metabolic rate is elevated, in severe anemia there is a deficiency in oxygen transport to the tissues, and in cor pulmonale there is a much diminished oxygen supply to the tissues due to a lowered arterial oxygen saturation of the blood As a consequence of this inadequate oxygen supply the heart muscle itself is affected and its contractile efficiency is reduced

Most of the patients in the first group exhibit the functional characteristics of hearts located on the decline or failure zone of the Starling curve as a fall of the venous pressure produces a rise in cardiac output Most of the patients in the second group have hearts whose functional characteristics place them on the upward slope of the Starling curve A fall in venous pressure produces a fall in cardiac output

METHOD OF TREATMENT

The measures used in the treatment of heart failure are designed to reduce the metabolic load on the heart or to increase the heart output In the first category are rest, control of fever or infection, and specific treatment for hyperthyroidism, beriberi or anemia The second category includes digitalis, which by direct action on heart muscle and indirect action on venous pressure increases cardiac output, and the diuretics, whose effect on sodium excretion reduces blood volume and venous pressure It is important to understand that when the metabolic load on the heart is excessive, as in hyperthyroidism, measures designed to increase the cardiac output further, such as digitalis, are most often ineffective unless the metabolic disorder which has caused the heart failure is treated

We will consider first the action of each of the measures used in treatment and the technic of its application Finally we will apply these basic therapeutic measures to specific types of heart failure

Rest and Restriction of Activity —The effects of rest on the normal heart are to decrease the demands of the body for oxygen, to reduce the heart rate and to increase the flow of blood through the kidneys These same effects are noted in the failing heart and sometimes without any other treatment patients will have great relief of the symptoms of cardiac failure by rest alone Diuresis will follow the increase in renal

blood flow with a consequent reduction in blood volume and venous pressure With the functional state of the heart on the decline of the Starling curve, the effect of rest is to cause an increase in cardiac output as a result of the drop in venous pressure

Rest should be mental as well as physical Patients who are put to bed because of early heart failure should be permitted time to arrange their business affairs, in order to avoid mental strain during their enforced inactivity When patients have much dyspnea and pulmonary congestion it is wiser to have them rest in a comfortable chair and even sleep in the chair if necessary In recumbency there is a marked shift of blood from the venous channels in the extremities to the lungs, with increase in pulmonary congestion It is best to have the head of the bed raised when a patient with heart failure is bedridden It is also wise to raise the foot of the bed a little so that the patient does not slide down and by bending the neck increase the difficulty in breathing Use of the commode may require less exertion than use of the bed pan

Rest should be ordered as a temporary measure The patient will understand how reducing the work of the heart by rest will help him to restore heart function and in the end lose less time from work In the beginning visitors should be restricted, but listening to the radio may be permitted for diversion Rest should not be prolonged beyond the point necessary to relieve the most disturbing clinical syptoms of failure or to insure recovery from the disease which may have induced the heart failure, such as cardiac infarction Prolonged rest brings with it the dangers of venous thromboses in the extremities and of pneumonia

After the patient has had an initial period of rest in bed and is able to carry on restricted activity without symptoms of failure he may be permitted to return to work At this point it will be necessary to decide whether a change of vocation is necessary or whether it is possible for the patient to carry on in his usual business or profession with some restriction in activity This is a difficult decision to make and many factors must be considered Of most importance are the cause of the heart failure, the natural history of the underlying heart disease, and the ability of the patient to carry on a life of restricted activity A man should not be told to give up his profession or business because of an attack of nocturnal dyspnea due to hypertensive heart disease or the signs of early heart failure which is often seen in the fourth decade of life in healed rheumatic heart disease Neither should a patient with heart failure which follows a first bout of cardiac infarction be encouraged to undertake new business ventures or to continue in those which require more than a moderate amount of exertion

When a patient is permitted to return to work he should be told to avoid, for a considerable period, all exertion not essential to his earning

a living. Evenings should be spent at home. He should retire early and arrange to have twelve hours of rest in each day whenever possible. There is no plan of restriction of activity which will fit all patients. The goal should be rest for the heart and reduction in metabolic needs. But the personality of the patient must not be overlooked in planning the regimen.

Oxygen Therapy.—When cyanosis is present in heart failure as a result of lowered oxygen saturation of arterial blood then oxygen therapy may be helpful in relieving dyspnea and at times may cause diuresis.[2] In the absence of cyanosis, however, I have not seen much benefit from oxygen therapy in heart failure.

Diet.—In the treatment of heart failure diet has attained a place of importance equal to that of digitalis and mercurials. Its importance cannot be overemphasized. It is most often the factor which makes for success or failure in treatment. The purpose of dietary treatment in heart failure is to reduce the metabolic requirements of the body and to

TABLE 1

KARELL DIET

8:00 A.M.	12 Noon	4:00 P.M.	8:00 P.M.
250 cc. milk	250 cc. milk	250 cc. milk	250 cc. milk

increase the output of the heart, if possible. The reduction in basal metabolic rate can be achieved by a semistarvation diet. As a result of this reduction, the heart rate is slowed and there is less work for the heart. Weight reduction is advisable in most patients as a further means of reducing metabolic demands. The Karell diet has been found to be ideal for this purpose and is more popular now than ever. The constituents of this diet are given in Table 1. The chief virtue lies in the fact that it is easily taken, rarely causes digestive disturbances, contains very little sodium and is low in calories and protein. It is taken by most patients without complaint at the beginning of treatment for heart failure. It may be given for three to five days and then replaced by a modified Karell diet (Table 2) or a low sodium maintenance diet (Table 3).

In the presence of reduced renal blood flow in heart failure, the extreme reduction of sodium in the maintenance diet will cause absorption of much less sodium and water by the intact renal tubules. As a consequence, the circulating blood volume and venous pressure will be reduced. In most patients with heart failure whose functional state is beyond the peak of the Starling curve in the zone of failure, it is apparent how this reduction in venous pressure will cause increased cardiac output, greater renal blood flow and less sodium retention, with relief of the edema and of the signs of congestion.

TABLE 2

MODIFIED KARELL DIET

8 00 A M	12 Noon	4 00 P M	8 00 P M
Fruit juice Salt-free bread with sweet butter 250 cc milk	Baked potato Stewed fruit Salt-free bread with sweet butter 250 cc milk	Stewed fruit 250 cc milk	Cream of rice cereal or Rice cereal Stewed fruit 250 cc milk

Coffee or tea may be added to the milk if desired

TABLE 3

MONTEFIORE HOSPITAL LOW-SODIUM DIET (500 MG OF SODIUM)

FOODS ALLOWED

Soup Vegetable, cream soups made with dialyzed milk

Meats Beef, lamb,* mutton,* calves' liver,* pork, veal, chicken, duck, turkey (preferably breast meat)

Dairy Products Pot cheese and cottage cheese (to be washed three or four times in hot water before using)
Whole milk ½ cup daily, or dialyzed milk ad libitum
Cream Sweet cream 2 oz daily (¼ cup)

Eggs One a day (or two, if one is substituted for a serving of meat or cheese)

Vegetables (fresh only) Asparagus, green beans, broccoli, cabbage (raw), cauliflower, corn, cucumbers, eggplant, peas, white potato, sweet potato, tomato, yellow turnip, endive, fresh lima beans, brussel sprouts, green peppers, all kinds of squash, carrots

Breads Salt-poor white bread, Passover matzoth

Cereals Rice, puffed rice, cream of wheat, shredded wheat, puffed wheat, rolled oats, wheatena, tapioca, Mead's cereal, Ralstons, pearl barley, macaroni, spaghetti

Desserts Fruits—apples, apricots, bananas, blackberries, blueberries, cherries, cranberries, dates, fresh figs, grapejuice, grapes, grapefruit, lemons, oranges, peaches, pears, pineapple, plums, raspberries, strawberries, watermelon, cider, fresh currants, huckleberries, rhubarb, prunes, tangerines, tapioca and rice pudding (made with dialyzed milk), gelatin made with water and fruit juice

Beverages Tea, coffee, cocoa, tomato juice without added salt, fruit juices

Miscellaneous Sweet butter, jelly, fruit jam and marmalade, olive oil and other vegetable oils and shortenings, white and light brown sugar, maple syrup, nuts (raw or plain roasted) —chestnuts, pecans, almonds, brazil nuts, cashew nuts, peanuts, hazelnuts, walnuts, unsweetened chocolate

* Indicates once weekly

The low sodium diet is not entirely free from danger, although I have seen very little harm come from its use After long adherence to this diet patients may become weak and easily fatigued Relief is obtained by the

addition of sodium to the diet Uremia may develop in patients with impaired renal function as the result of very low sodium diet Such patients require special care and observation [9]

Water intake need not be limited if salt intake is restricted Low sodium diets which permit 4 to 5 liters of water daily are used in cardiac failure, sometimes with good effect I have not found this Schemm diet popular with my patients, but I do allow patients to take enough water to avoid the discomfort of thirst.

If patients are very hungry on the Karell diet, an additional pint of milk may be added Additional water may be taken if desired I have kept patients on this diet without modification for three to five days The more severe the failure the greater the necessity for this diet After a few days a modified Karell diet may be used (Table 2)

When a salt free diet is prescribed it is not enough to caution in a general way against the use of salt in food It is necessary to specify precisely what a patient may eat Diets taken by patients without precise directions usually contain much more sodium than is desirable Therapeutic results cannot be expected from a prescription to avoid salty foods or the addition of salt to food

Digitalis—Digitalis has been used in clinical medicine for the past 150 years as the principal agent in the treatment of heart failure However, there is still considerable difference of opinion concerning the mode of its action on the failing heart Its action on the normal heart in man is clear It reduces the venous pressure, the size of the heart and the cardiac output

In general it may be said that in heart failure with low cardiac output, the common type of heart failure, digitalis *lowers the venous pressure* promptly after its injection With the drop in venous pressure the cardiac output rises With the rise in cardiac output the renal blood flow is increased and diuresis follows, with a reduction in blood volume and relief of the symptoms of venous engorgement

It is established that digitalis acts to increase the force of *contraction* of mammalian heart muscle in failure Many workers believe that this increase in the force of contraction is sufficient to explain the rise in cardiac output and all the benefits to the circulation which follow this augmented output Others believe that the principal action of digitalis is to lower the venous pressure With a *drop in venous* pressure during heart failure a rise in cardiac output occurs and all the benefits to the circulation follow How *digitalis acts to cause this fall in pressure* is not known [10]

Digitalis also slows the heart rate by an increase in vagal tone and by direct effect on the conduction system The slowing of the ventricular rate in auricular fibrillation and the occurrence of heart block from

digitalis action are the best known effects of the drug It can readily be seen that a reduction in ventricular rate allows for a longer period of diastole in each contraction more rest for the heart muscle and a better diastolic filling of the coronary vessels This increases the efficiency of the heart muscle This effect of slowing is added to the direct effect on the venous pressure All these effects together cause the rise in cardiac output

Digitalis is effective also in the treatment of heart failure with regular rhythm The slowing of the heart is less evident, especially when the rapid heart rate is due to some cause other than the heart failure, such as fever or infection When the rapid regular rate is due to the failure itself, then a slowing of the rate may be expected as a result of the effect of digitalis on the venous pressure The slowing is more evident and more salutary in patients with auricular fibrillation The effectiveness of digitalis in cardiac failure seems to diminish with the passing of time Its most brilliant effects are seen in early heart failure When the heart muscle becomes altered physically and chemically by long-standing failure, it is less responsive to the effects of digitalis The same lack of response to digitalis is seen in the failure of acute rheumatic fever when the heart muscle is severely damaged

The toxic effects of digitalis are well known and include loss of appetite and mental changes as early evidences of digitalis poisoning It is best to stop the drug when the toxic effects are noted, since we are no longer entirely dependent on digitalis for the treatment of heart failure Diuretics can nearly always be used to tide the patient over any period when toxic symptoms appear It is my experience that during the past few years more patients have had to be treated for digitalis poisoning than ever before This is due to the fact that the very potent glycosides are in more general use and that there is still no agreement as to dosage A recent paper by Master[11] records his experience with digitoxin I have seen the same effects from digitoxin on my hospital service It is safer to use 0 1 mg for maintenance of digitalis effect, unless a patient cannot be controlled by this dose I have less difficulty with toxic effects when I use the products of *Digitalis lanata*

Administration — I prefer the use of the pure glycosides They are less irritating to the stomach than the whole leaf, and can be taken without discomfort by nearly all patients Digitoxin is absorbed completely from the stomach and exerts its full effect in six to ten hours Cedilanid and digoxin are absorbed much less completely, but have a shorter latent period of action and are excreted more rapidly than digitoxin For very rapid action in rare instances it is necessary to inject strophanthin K or ouabain intravenously (Table 4)

I have found digitoxin best for producing initial digitalis effect and either cedilanid or digoxin best for maintenance

Diuresis—The retention of sodium and water in heart failure is responsible for edema which may be present in the lungs or in any tissue in which the tissue pressure is low enough to permit accumulation of fluid The removal of this fluid by diuresis causes a reduction in blood volume and venous pressure with relief of symptoms due to venous congestion The most effective diuretics are the salts of mercury Mercury acts by reducing the power of the renal tubules to absorb sodium and

TABLE 4

DOSAGE SCHEDULE

For Emergency Use (Ampoules)	Strophanthin K	0 25 mg by vein
	Ouabin	0 25 mg by vein
	Cedilanid	0 80 mg by vein

This dosage may be repeated once in twelve hours It is not safe to use these products if digitalis has been taken in the recent past After digitalis effect has been obtained, then oral dosage for maintenance is started

For General Use (Oral Tablets)	Digitoxin	0.2 mg and 0 1 mg Total dose for initial digitalis effect is 1 0 to 1 4 mg, depending on weight of patient May be given in one dose if necessary
	Cedilanid	0.5 mg Total dose for initial effect is 5 mg in divided doses over a period of 3 to 5 days
	Digoxin	0 25 mg Total dose is 7.5 to 10 mg in divided doses
For Maintenance of Digitalis Effect (Oral Tablets)	Cedilanid	0.5 mg 1 or 2 daily
	Digoxin	0 25 mg, 1 or 2 daily

water Aminophylline is an effective diuretic which may be used to increase the effect of mercury [17] When given by vein or in a rectal suppository it increases the renal blood flow Ammonium chloride may also be used in doses of 6 to 8 grams daily to enhance the effect of mercury The other diuretics of the xanthine and urea groups are falling rapidly into disuse I have not used a diuretic of either type for many years

After an effective diuresis by mercury alone, or in combination with aminophylline or ammonium chloride there is striking relief of congestion in the lungs with lessening of dyspnea and cardiac asthma The engorgement of the liver and viscera is reduced and ascites often disappears without necessitating paracentesis I have not seen resorption of pleural effusion resulting from the use of mercurial diuretics, but it has

been reported by others [4] I have seen much relief obtained by injection of mercurial compounds in severe failure of acute rheumatic fever and also in heart failure after cardiac infarction I share the opinion expressed by Fishberg[6] concerning the hazards of mercurial diuresis in the period following cardiac infarction, when shock dominates the clinical picture

Mercury should not be given to patients who have edema caused by acute nephritis It is also unwise to inject mercury in the presence of severe renal insufficiency from any cause Renal shutdown may follow It is well to remember that the diuretic effect of mercury is retarded somewhat by morphine and other drugs of similar action The heavy albuminuria due to failure, however, is no contraindication to the use of mercury

In the treatment of heart failure during the last decade mercury has replaced digitalis as the most effective agent This is especially true in the treatment of heart failure of long duration Whenever mercury is necessary as a diuretic it is most effective when given intravenously or intramuscularly When given by vein mercury may cause severe reactions, and the deaths from mercury which I have seen occurred after intravenous administration Intramuscular injection made carefully is quite safe and effective and causes only slight pain I have no experience with oral tablets, but they are recommended It is best to start with a dose of 0 5 cc of any mercurial diuretic combined with theophylline for the first intramuscular injection After this probatory dose is found safe, then 1 to 2 cc may be given daily if necessary to obtain relief of distressing pulmonary congestion I believe the need for rapid removal of pulmonary congestion is the principal indication for the use of mercury

Since I have used a strict low sodium diet in my practice I have had much less need to use mercury as a diuretic In a panel discussion in June, 1947, White stated that during the past few years he has been able to dispense with mercurial diuretics altogether or to use them infrequently in many of his patients with myocardial failure This has been my experience also

SPECIFIC TYPES OF HEART FAILURE AND THEIR TREATMENT

In the type of heart failure which is most common there is usually evidence of antecedent heart disease and an additional precipitating factor If this factor is exertion, this must be controlled If infection is present it must be treated immediately

The dominant signs and symptoms may appear in the lungs only or in the liver and viscera, depending on the site of the principal damage to the heart muscle Thus, at the onset, in heart disease due to hypertension, coronary artery disease or syphilis the picture of left heart failure is

dominant. In rheumatic mitral disease or cor pulmonale the picture of right heart failure is in the forefront With time this distinction is less evident, and the phenomena of increased venous pressure and edema are present both in the lungs and in the viscera

Most of the hearts in this group are located on the downward slope of the Starling curve so far as their functional capacity is concerned Rest, low sodium diet and digitalis all act to lower the venous pressure by the mechanisms described above With a drop in venous pressure there is a rise in cardiac output The rise in output further increases the renal blood flow, decreases the blood volume and further lowers the venous pressure In most of these patients no other treatment is necessary, certainly not at the beginning of heart failure

There are acute episodes of heart failure which require somewhat different treatment The most common of these is the episode of acute nocturnal dyspnea or pulmonary edema which is often seen in patients with hypertension In such patients, after a small dose of morphine has allayed anxiety and there is no doubt about the diagnosis, a full digitalizing dose of a glycoside should be given, followed in the morning by a probatory dose of 0 5 cc of a mercurial If there are no untoward effects from the mercurial than 1 cc may be given the following morning if necessary The patient should be put at rest, given a Karell diet for three days and his weight recorded After this a modified Karell diet or a sodium free diet is given The weight is recorded every day Digoxin or cedilanid is given daily When the patient has reached a stage in which there is no weight change, no dyspnea, no evidence of pulmonary congestion and no edema, the recorded weight may be considered to be the dry weight of the patient An attempt should be made not to exceed this weight by more than a few pounds at any time As soon as there is an appreciable weight increase the patient should take a Karell diet for three days with 2 grams of ammonium chloride three times a day This usually suffices to bring the weight back to the dry weight If not, a dose of 1 cc. of mercury will usually help One of my patients with rheumatic heart disease and auricular fibrillation has followed this regimen for the past five years, keeping his weight between 115 and 118 pounds He has not had to resort to mercury during this entire period, although before this regimen was started he had had a mercurial injection every week for a number of months

It is not necessary to restrict water at any time during treatment nor is it necessary to measure the intake and output of fluids An accurate weight record is much less subject to error It is necessary to have an accurate scale available at all times Occasionally a slow gain in weight may mean actual gain in flesh and not edema fluid In such cases the

regimen described above to remove occult edema will usually cause very little loss in weight

Most patients with chronic heart failure can be kept comfortable and many patients are restored to useful activity by the method of treatment outlined above It is clear that the stress is laid on the maintenance of the dry weight by the use of a sodium-poor diet and digitalis, aided by periods of Karell diet and administration of ammonium chloride when there is a tendency for the weight to rise much above the dry weight It should be pointed out that mercury is only rarely necessary It is possible to accomplish the same by measures which are safer and easier to apply

There is a group of patients with heart failure who do not respond well to the treatment outlined above The most frequent examples are patients with hyperthyroidism and chronic cor pulmonale Patients in this group have heart failure only after years of brave effort on the part of the heart to meet the much increased metabolic demand In my experience patients with hyperthyroidism do not have heart failure before middle age Almost always these patients have auricular fibrillation of long duration The usual measures, including digitalis, have little or no effect on the control of heart failure unless the hyperthyroidism is treated In patients with chronic cor pulmonale it is usually impossible to alter in any significant way the underlying pulmonary disease and the consequent ventilation insufficiency For this reason, despite our best efforts, patients with cor pulmonale do not respond well to treatment when heart failure is present In this group of patients the stress is laid on the removal, whenever possible, of the excessive demand on the heart When this is accomplished, as in the operation for the obliteration of an arteriovenous shunt, the signs of heart failure disappear without any other treatment

It has been pointed out that successful control of the clinical signs of heart failure does not necessarily mean an improved circulation [1,15] Most patients require continuous treatment by limitation of activity, low sodium diet and digitalis Those patients whose heart failure is the result of some acute cardiac injury or excessive extracardiac demand may be able to resume normal living after recovery without further treatment

SUMMARY

Heart failure may be defined as a state in which the heart is unable to maintain a circulation sufficient to meet the metabolic demands of the body This may be due to the fact that the heart muscle is diseased and as a consequence the cardiac output is less than that of the normal resting heart Or it may be due to an excessive metabolic demand upon a normal heart muscle which is able to respond with an increased cardiac

output, but which fails ultimately if the metabolic demand is not decreased

Our purpose of treatment in low output heart failure is to increase the output of the heart by rest, diet, digitalis and diuretics The purpose of treatment in high output failure is to remove the metabolic need for the high cardiac output.

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STREPTOMYCIN TREATMENT OF TUBERCULOSIS ITS DOSAGE, INDICATIONS AND CONTRAINDICATIONS

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STREPTOMYCIN represents a great forward step in the treatment of tuberculous disease in man Its value can be best utilized by recognition of its chief indications and contraindications and of the optimal dosage and manner of administration Many problems concerning these have not yet been completely solved, but much has been learned with regard to them in the few years since this treatment first became available One of the first patients treated with streptomycin at the Olive View Sanatorium illustrates many of the important points in connection with this treatment

ILLUSTRATIVE CASE

Mrs E W , a 35 year old white woman, became ill with an insidious onset in April 1944 with cough, expectoration, anorexia, loss of weight and fatigue, accompanied by low fever and night sweats X-ray examination on July 28, 1944 revealed scattered, bronchopneumonic, patchy lesions throughout the upper and lower half of the left lung with at least two cavities in its upper lobe and an extensive bronchopneumonic confluent infiltration in the upper lung field on the right with multiple cavities in the first and second interspaces The diagnosis of tuberculosis was confirmed by a finding of positive sputum

After continuous institutional treatment with bed rest for more than two years there had been considerable clearing of the disease since the original x ray examination There remained extensive nodular lesions in the upper half of both lung fields with a small cavity in the left first interspace and a large one more than 6 cm in diameter, on the right Repeated bronchoscopic examinations demonstrated extensive tuberculous ulceration and granulations of the lower third of the trachea Streptomycin chloride (2 gm dissolved in 5 cc of distilled water), divided into five doses was administered daily from January 21, to January 26, 1947 At that time the patient had developed marked vestibular disturbances and streptomycin blood assays showed over 80 micrograms of streptomycin per cubic centimeter of blood, which was far above the therapeutic levels of 10 to 20 micrograms desired Accordingly, treatment was diminished to 1 gm of streptomycin given in two doses daily and continued to March 4 1947 for a total of six weeks' treatment

Although the eighth nerve symptoms, especially dizziness and tinnitus aurium persisted and increased the patient's general condition improved under this treatment Bronchoscopy February 21 showed apparent subsidence of the

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tracheobronchial lesions with reddening and thickening but no ulcerations or granulations remaining The sputum, which had been continuously and heavily positive previously, decreased in volume but remained positive to culture Three weeks after discontinuance of the streptomycin the patient's wheezing and cough returned Bronchoscopy on March 28, 1947 showed no change in the old tracheal lesion but a new fresh tuberculous lesion in the right intermedius bronchus

Streptomycin, 0 5 gm daily in a single injection, was accordingly started April 1, 1947 and continued until July 19, 1947 Bronchoscopy June 11 showed improvement though some active disease still remained in the right main bronchus On July 16, 1947 bronchoscopy was reported as showing complete healing and later bronchoscopies have confirmed this finding The sputum, which had been consistently positive before streptomycin treatment, diminished in volume and number of bacilli, and became microscopically negative by June 20, 1947 The last positive culture, which was obtained on July 15, 1947, proved to be completely resistant to the influence of streptomycin

Since x-ray study showed apparent disappearance of the cavity on the left side but increase in the cavity with a large fluid level on the right, artificial pneumothorax was tried, but it was unsuccessful and pneumoperitoneum, induced on August 20, 1947, was maintained for only one month On September 23, 1947 a first stage right thoracoplasty was performed Following it there was an increase in symptoms Repeated bronchoscopies showed no definite tuberculous lesions or obstructions but a large amount of secretion was aspirated A roentgenogram on October 1, 1947 showed an increase in the soft lesions in the right midlung under the thoracoplasty Streptomycin was, accordingly, started again, 1 gm daily from October 3, 1947 to October 19, 1947 The second stage of thoracoplasty was performed under local anesthesia on October 27, 1947 The last culture had shown the last organisms obtained from this patient to be resistant to streptomycin and x-rays showed little response to the streptomycin treatment of her postoperative spread, although she had shown some symptomatic improvement Promin, 4 gm in 10 cc of dextrose solution, administered slowly intravenously, and moogrol, 2 cc in oil intramuscularly, daily, were started on October 28, the day after the operation, and continued to January 19, 1948, a total of nearly three months During the six months following operation the patient had made a relatively slow but uneventful convalescence X-rays show no evidence of remaining cavitation and the nodular densities remain unchanged More than a score of sputum cultures including several gastric lavages have been negative and the patient is essentially afebrile and asymptomatic She is now being advanced from the complete bed rest regimen, being slowly made ambulatory in the hope that her convalescence and eventual rehabilitation may proceed uninterruptedly She has gained in appetite, weight and general well-being and shows no further evidence of any active tuberculous disease Her hemoglobin has risen from 60 per cent following admission to 80 per cent in more recent months

Although bed rest continuously for a period of a number of years had stabilized some of the soft pneumonic lesions in this patient's lung, she

required special additional treatment for complications The tuberculous tracheitis responded well to streptomycin treatment and a later tuberculous bronchitis also responded to a subsequent course of the same drug The large cavity showed little change as a result of this treatment although sputum lessened and cultures became negative, hence pneumoperitoneum followed by thoracoplasty was utilized to control this lesion

An increase in the disease following the first stage apparently subsided Whether the additional streptomycin treatment or the long-continued promin and moogrol administration contributed to this result may be open to question, since postoperative spreads often subside without requiring such measures The fact that the large dose of 2 gm a day produced toxic symptoms in this patient, that the tracheobronchial lesion responded to streptomycin in doses of 0.5 gm as well as 2 gm, and the necessity for additional collapse therapy and chemotherapy with or following the streptomycin treatment are well brought out, however, in this history

DOSAGE AND ADMINISTRATION

The value of streptomycin in the treatment of many forms of clinical tuberculosis has been established There is still insufficient data on record as to just what dosage is necessary to achieve optimal results Patients have been treated with more than 3 gm in a single intramuscular injection Others have received as much as 10 gm in twenty-four hours by continuous intravenous drip or multiple intramuscular injection Still others have received more than 3 gm daily for periods of many months With such high dosage toxic manifestations are almost uniformly present In the early days streptomycin was given by continuous intravenous injection and attempts were made to obtain continuous high blood levels by frequently repeated intramuscular injection as often as every two hours during the day and night The duration of a course of treatment has also been prolonged in some cases to more than a year Not only the tremendous expense of such heavy dosage and prolonged courses of treatment, and the amount of medical attention required in administering such prolonged and frequent treatments but the actual danger from marked toxicity to the patient and the lack of commensurate therapeutic gain made it advisable to determine whether small doses, less frequent injections and briefer periods of treatment might not be equally effective

In Vitro Effects. The majority of tubercle bacilli obtained from patients before treatment with streptomycin will not grow and multiply in the presence of one part of antibiotic in a thousand parts of media, or a

concentration of 1 microgram per cubic centimeter, and many are restrained by lower concentrations Rarely is any evidence of inhibition seen with concentrations below 0 1 microgram per cubic centimeter A level of 2 to 3 micrograms of streptomycin per cubic centimeter, then, may be expected to inhibit the growth of most tubercle bacilli in vitro

Streptomycin appears to be almost entirely bacteriostatic and not bactericidal to the tubercle bacillus Inhibition is noted immediately after the addition of large amounts of antibiotic to a growing culture of tubercle bacilli, but minimal amounts of streptomycin may produce only a gradual slowing of the growth rate for a number of days before growth actually stops completely This has also been reported with penicillin and sulfonamides Despite intimations from animal experiments and clinical experience, there is no indication from in vitro experiments of any residual inhibiting effect of streptomycin on the tubercle bacilli after the antibiotic is completely removed

Blood Levels vs. Dose in Animals.—Streptomycin blood levels in experimental animals injected with varying amounts of streptomycin were determined by a modification of Forgacs' bio-assay technic, using Bacillus subtilus spores in agar medium in flat Petri dishes and plating with bacteriologic loop by a method similar to that described by Levine The results are less precise than would be expected with more elaborate methods, particularly the chemical tests, but generally yield concordant results In general, the streptomycin concentration in the whole blood, taken two hours after an intramuscular injection, was proportional to the amount given to any individual—and approximated the total dose divided by the body weight Thus, when guinea pigs of different sizes were given the same dose of streptomycin, the smaller ones showed higher concentrations of streptomycin in the blood However, if the dose was calculated according to weight the reverse was observed, and the larger animal showed somewhat higher concentrations in the blood stream

Streptomycin is distributed somewhat unevenly throughout the body, the concentration in various tissues and fluids being apparently related to their fluid content It has been suggested that the streptomycin in the entire body is contained only in the liquid portion Even in the blood, streptomycin is found in the plasma rather than in the cells Studies of the theoretical peak concentration after injection, as reported by Boxer, indicate that the concentrations obtained in the blood serum are similar to those which might be expected to occur if all of the streptomycin were distributed in about a quarter of the total body weight, or in the free fluid in the body, rather than equally throughout the tissues Physiologic anatomic studies have shown that the blood volume, and probably also the general fluid volume in the body, is proportional to the body surface, rather than to the body weight, and does not increase as rapidly as does

the skeletal or total body weight Accordingly, small animals have relatively more blood than have large ones When we speak of the average blood volume of a man being about 12 per cent of total weight this is merely an approximation In a small person or child a higher proportion of blood might be found, while in a giant or a large person, particularly one with much fat, the relative blood volume would be less The actual blood volumes seem to be more nearly proportional to the two thirds or three-quarters power of the body weight When dosage calculated proportionate to the two thirds power of the body weight was administered to the animals, no differences between concentration in large and small animals were noted

Comparison of the blood levels with the body weight in a group of 100 patients showed a rough correlation The heavier patient showed lower blood levels and the smaller patient showed relatively higher levels with the same dose However, the increase was not directly proportional to the dose per kilogram but somewhat less, suggesting confirmation of the findings already made on animals that the blood level is proportional to the blood volume or body surface area rather than to the body weight itself There was considerable variation in the blood values obtained, due in part to the variations in body size of the patient and in part to the occurrence of patients with definite renal insufficiency, where inordinately high figures were obtained In spite of the admitted lack of precision of these dilution methods, it would appear that there is considerable variation in the blood level of streptomycin following similar dosage in a group of individuals of the same size Unfortunately, adequate data based on chemical determinations of the blood concentrations in patients of different weight, receiving different size dosage are not yet available here, but it is hoped that they may be obtained in the future

Maximum Limits of Dosage—Lethal dose levels of streptomycin have been recorded for a number of species of animals Large animals withstand higher doses than small ones If the dose given is directly proportional to the body weight, however, larger animals may be affected more than are the smaller ones Clinically, vestibular toxicity has also been more marked in small patients when a uniform dose has been given to all, but in large men, when the dose given is a direct product of the body weight If the toxic dose were a function of the total body fluids or of the blood volume rather than of the body weight, it would also be more nearly proportional to the two thirds or three fourths power of the weight than to the weight itself

On the basis of animal experiments it may be calculated that from 10 to 20 gm of streptomycin injected intramuscularly at one dose would be the average fatal dose for a human being Smaller doses than this would then be the minimal lethal dose in sensitive individuals or with more toxic

preparations Actually as much as 3 gm of streptomycin have been given patients at a single time and even larger amounts divided into many small doses during each day have been taken by many patients for several months without a fatality Although 400 mg of streptomycin sulfate per kilogram is about the average lethal dose for adult guinea pigs of around 1 kg in size, smaller animals withstand more and larger animals less dosage per weight, baby guinea pigs surviving two or three times this concentration (Table 1) With the less toxic streptomycin calcium chloride complex, about 50 per cent more streptomycin is needed to kill the animals

Romansky reported that intraspinally injected streptomycin causes severe irritative phenomena if given in concentrations greater than 1 mg per kilogram of body weight in dogs, and advised that this should be the maximum ratio allowed in patients Human patients have also generally shown irritative phenomena with about double this dosage

Animals usually died about an hour after the inoculation of doses of approximately 400 mg per kilogram, which might be expected at this

TABLE 1

AVERAGE LETHAL DOSE OF STREPTOMYCIN SULFATE IN GUINEA PIGS

Wt of Guinea Pig in Gm	Lethal Dose, Mg per Kg
800+	380
400 to 800	440
−400	500

time to give blood levels of 400 micrograms per cubic centimeter Blood levels found in rabbits killed with an overdose of streptomycin were generally somewhat below those found on the guinea pigs More work on lethal blood levels is desired Blood levels after fatal doses of streptomycin sulfate in experimental guinea pigs and rabbits range from 300 to 1000 micrograms per cubic centimeter This would represent what might be expected with doses of about 300 mg per kilogram or about 15 gm in an average man Moderate but continuously sustained concentrations of streptomycin in blood seem more apt to be associated with renal irritation and impairment and vestibular damage and other toxic manifestations than are high peaks with intervening low levels Doses of 3 gm or more at a time in man are more apt to be associated with paresthesias and other discomforts than the same amount in divided doses during the day Similar data has not been reported on animals except perhaps in the case of fatal dose levels where high peaks may be more dangerous

Therapeutic Dosage in Guinea Pigs —On the basis of experience with penicillin it was concluded that antibiotic agents generally must be present in higher concentration in the blood stream than is necessary to

inhibit susceptible organisms in the test tube in order to obtain effective inhibition in vivo Since experiments indicate that the administration of *1 mg of streptomycin per kilogram of weight of animal results in peak* blood concentrations of about 2 micrograms of streptomycin per cubic centimeter of blood in the animal, but that the concentration in the blood *diminished by about half every two or three hours, it might be expected* that a dose of at least 0 33 mg per kilogram per hour, or about 10 mg per kilogram per day, would be required to maintain blood levels of 2 to *3 micrograms of streptomycin per cubic centimeter*

Animal experimenters have been apt to give streptomycin in terms of dose per kilogram of body weight of the animal, so that a dose of 1 mg given to a mouse of about 2 ounces in size, or about 15 mg a kilogram, may be compared to about 10 mg to a guinea pig weighing 1½ pounds, or about 50 mg for an 8 pound rabbit

TABLE 2

STREPTOMYCIN DOSAGE IN TUBERCULOUS GUINEA PIG

Av Daily Dose Mg per kg	No of Guinea Pigs	Per Cent Reduction in Tb
1 to 4	55	33
5 to 9	45	67
10 to 19	118	74
20 to 35	24	86
35 to 100	24	90

Experiments indicate that daily dosage of 10 to 20 mg per kilogram of weight almost completely inhibits the development of tuberculosis in inoculated animals Some retardation in the development of tuberculosis in these animals was observable with smaller dosage As little as 1 mg of streptomycin per kilogram per day gave only a trace of effect but 2 or 3 mg of streptomycin per kilogram per day in guinea pigs produced detectable retardation of the disease, though far from the amount of inhibition shown by larger doses The therapeutic effect in experimental animals increased with increased dosage up to 10 or 20 mg per kilogram (Table 2)

In spite of theoretical expectation, the therapeutic effect of streptomycin in experimental animals seems to be exerted, on the tubercle bacillus at least, by high peaks and intervening low blood levels as well as by continuous moderate blood levels with persistent exposure of organisms to its action With the same total daily dosage of the agent the reverse has generally been accepted as true for penicillin Recent reports cast doubt on this earlier belief as it has been found both clinically and in experimental animals that infrequent injections of rapidly absorbed

aqueous solutions may be as effective therapeutically as more frequent injections or more slowly absorbed preparations, even though blood levels rapidly decline In earlier experiments guinea pigs were given treatments every few hours, but the published studies by Feldman and more extensive guinea pig investigation at Olive View indicate that not only is a single daily dose as effective as the same amount of drug given in divided doses, but injections once a week or even once in two weeks may be similarly effective if sufficient streptomycin is given to each animal Perhaps the transitory inhibition by the antibiotic agent allows physiologic and immunologic mechanisms within the body, such as phagocytosis and immobilization of the organisms, to occur even within a few hours and this combined effect may be more lasting than the direct

TABLE 3

STREPTOMYCIN DOSAGE

Daily Dose	No of Cases	Per Cent Improved	
		Local Lesion	Chest X-ray
2 0 gm intramuscularly	32	90	53
1 0 " "	60	86	58
0 5 " "	47	83	53
0 2 " "	36	73	50
0 1 " "	41	48	44
Local	62	44	45
0 (Control)	100	48	50

bacteriostasis seen in vitro However, it may be explained, it appears that frequent dosage of streptomycin is clinically unnecessary and may be even inadvisable

Studies both on experimental animals and in patients, have yielded extensive data regarding minimal, maximal and optimal therapeutic daily dosage and individual dose, and frequency of administration Peak blood levels of about 4 micrograms per cubic centimeter, such as are found in patients after the administration of 0 1 gm or in animals after receiving about 2 mg per kilogram, appear to be the least which will exert any detectable effect against tuberculosis Optimal results are obtained at about five times these figures, with blood levels of 20 micrograms per cubic centimeter such as are obtained by giving 10 mg per kilogram or about 0 5 gm per day in man Increasing the dosage above these figures gives little improvement in results Tabulation of the results of treatment in hundreds of courses of streptomycin treatment observed in patients of Olive View Sanatorium support these conclusions (Table 3) Doses of less than 0 1 gm per day are entirely without effect Doses

between 0 1 and 0 2 gm infrequently yield any detectable response The effectiveness increases between 0 2 and 0 5 gm but above this dosage no improvement is noted in the results achieved

Treatment of Resistant Forms. When resistant forms of tubercle bacilli appear in patients under treatment, they usually soon show such high tolerance to streptomycin that increasing the dose in the hope of affecting them is futile Clinical experience has also proved that they cannot be prevented by initially large doses

The duration of treatment is also disputed When the resistance may be ascertained, it may be safe to continue as long as susceptible forms predominate, but there seems to be little advantage in so doing Treatment of resistant organisms is useless and may be harmful The greatest clinical symptomatic effect is noted within the first month, but the improvement as shown by x rays is most marked in later months and sputum conversions may still occur even later Clinical relapses and reversion to positive sputum often follow discontinuance of treatment, but may also occur during the third and fourth month of treatment Treatment for tuberculous meningitis is still generally being carried on for six months and more, but for most other conditions the duration of treatment is being shortened from the earlier four or three months to the six weeks now being tried in the Veterans Administration, or even shorter if clinical indications point to satisfactory effect such as clearing of mucous membrane ulceration or cessation of drainage from a sinus

Despite expectation, it has not been demonstrable that any site or type of tuberculous lesion requires a larger daily dose of streptomycin than do others, although there may be differences in the duration of the course of treatment needed, and some lesions respond much better than do others Thus, draining sinuses or mucous membrane ulcers heal much more frequently and earlier than do old pulmonary lesions, but the lesions that do respond generally do so at the same daily dosage level

INDICATIONS FOR STREPTOMYCIN IN TUBERCULOSIS

In primary tuberculous infection, lesions are generally localized and closed and tend to encapsulate or resorb In such cases streptomycin is not indicated since it does not apparently accelerate the healing process. If primary lesions show evidence of progression, extension, spread or the development of complications such as adenitis pleural involvement and particularly hematogenous spread, a course of streptomycin would appear advisable

Minimal and moderately advanced cases of pulmonary tuberculosis which are active and not obviously regressing might also profit from a course of streptomycin But there seems to be no valid reason for giving

the treatment for inactive or regressing lesions Localized tuberculomas and blocked cavities in the absence of evidence of open active disease otherwise are apparently relatively unaffected by this treatment Streptomycin is particularly useful with very recent, fresh spreading disease It may well be given on appearance of such a lesion before waiting to find out whether it might not resolve naturally without the treatment, since the occurrence of destructive caseation necrosis may possibly be averted by the treatment in some cases Acute tuberculous infiltration, spills and spreads, such as occur after hemorrhage or operation, appear particularly suitable for streptomycin treatment, and even fresh tuberculous pneumonias often respond in a surprising manner

In the vast majority of cases of extensive, advanced pulmonary tuberculosis, streptomycin constitutes only a part of the treatment and is aimed especially at the control of acute spreading, exudative components Chronic fibrosis, cavitation and extensive caseation usually fail to respond to this agent The indirect effect of the streptomycin on cavities through its action on peripheral exudative lesions or tuberculous tracheobronchitis may sometimes occur, but is not to be relied upon Atelectasis, pleural effusions, fibrocaseous, calcific and destructive lesions are also not directly affected by the streptomycin

Inflammatory lesions of the bronchi, owing to the local irritation by sputum from tuberculous foci or secondary infection, may only incidentally, temporarily or symptomatically improve with streptomycin treatment, and may respond better to penicillin or to sulfones, or to mechanical measures aimed at the pulmonary lesions Granulating and ulcerative lesions of the visible bronchi, however, respond with a remarkably rapid and complete clearing Submucous infiltrations and especially fibrotic lesion with stenosis or weakening of the bronchial walls with resultant expiratory narrowing or external pressure may also fail to respond to streptomycin

Lesions due to intracanalicular spread of tuberculosis generally respond well to streptomycin treatment This seems to be true of early acute aspiration spreads in the lungs, of active bronchial or tracheal granulation and ulcerations and of laryngeal, pharyngeal, buccal or lingual ulcers, as well as of tuberculous enteritis and colitis On the other hand, pleural effusions may develop during the course of streptomycin treatment and the treatment appears to be generally ineffective both in pure tuberculous and mixed empyemas, irrespective of whether or not they may be complicated by bronchopleural or pleurocutaneous fistulas

Drainage from tuberculous sinuses, whether from tuberculous lymphadenitis, bone or joint involvement, or cold abscesses elsewhere in the soft tissues, generally diminishes promptly and soon ceases under streptomycin treatment and the sinuses themselves go on to closure and

healing The underlying lesions also usually show symptomatic improvement and regression, but their ultimate results depend upon the extent, age and nature of the lesion and its status at the time of discontinuance of treatment or on the occurrence of tubercle bacilli resistant to the antibiotic (Table 4)

CONTRAINDICATIONS TO THE USE OF STREPTOMYCIN IN TUBERCULOSIS

The most obvious initial limitations to the use of streptomycin—scarcity of the material and its high cost—have been practically overcome by improved and increased manufacturing facilities As a result,

TABLE 4

LOCAL LESIONS TREATED WITH 0 2 TO 2 GM OF STREPTOMYCIN

	No of Cases	Per Cent Improved
Tracheobronchial	31	94
Larynx	63	83
Draining sinus	25	82
Bone and genitourinary	23	83
Other	18	67

this agent, which could be produced only in milligrams in the bacteriology laboratory following its discovery in 1944 and reached a production of 2 kg per month in early 1946 when its distribution and control was undertaken by the Streptomycin Committee of the National Research Council, is now being manufactured in quantities of thousands of kilograms annually and being shipped to all parts of the world

Since it became commercially available, the price has dropped from more than forty dollars per gram to around two dollars per gram, and may sink even lower under the influence of competition, while the purity and stability of the product has continually increased Moreover, the lowering in the average dose of streptomycin used, from more than 2 gm to less than 0 5 gm per day, and the shortening in the period of treatment from many months to an average of less than two months further reduce the cost of the treatment Thus, streptomycin treatment now costs less than fifty dollars a course for most patients

The necessity for hospitalization and special nursing involved in the giving of the treatment by frequent intravenous injections every few hours was a further obstacle Some doctors attempted to circumvent this by teaching the patients themselves or members of their family to give the inoculation as often as every two hours during the day and night Further experience has shown that this is entirely unnecessary and that one treatment a day is ample Even one or two treatments a week may

be sufficient to obtain therapeutic response, if the dose given is large enough As a result, streptomycin may be given feasibly as an office procedure Not only is the cost of the medication and the cost of administration greatly reduced thereby, but the pain of frequent repeated needle punctures and sore spots is also obviated (Table 5)

The lower dosage now recommended has greatly diminished the toxic effects of streptomycin, which formerly constituted a great obstacle to its wider use Vestibular dysfunction and renal irritation with instances of total anuria which developed following treatment with high doses and high blood levels, and the rare instances of partial or complete deafness have been practically eliminated by the reduction in dosage Increased purification of the medication has also lessened the danger of histamine reaction and other toxic responses due to impurities

TABLE 5

FREQUENCY OF INJECTIONS WITH 1 GM DAILY

No of Daily Injections	No of Cases	Per Cent Improved	
		Local Lesion	Chest X-ray
5 or 6	24	83	58
3 or 4	19	85	58
1 or 2	17	87	59

Allergic sensitization with the development of eosinophilia, dermatitis and other manifestations are, however, encountered even with the smallest doses of the purest preparations Thus, they have even followed the infinitesimal exposures suffered by nurses or neighboring patients They may be so severe as to preclude the further administration of the treatment In a few instances sensitized individuals have exhibited anaphylactic shock symptoms on later intramuscular injections of the streptomycin The danger of developing such sensitization which would preclude the later use of streptomycin offers a substantial objection to its use in patients in whom it is not definitely indicated

The greatest limitation in the use of streptomycin is the appearance of resistant forms of tubercle bacilli in patients after they have been receiving the treatment for some time This not only represents the survival of preexistent resistant bacilli after the elimination of the great mass of susceptible organisms, but it appears to be accompanied by an absolute as well as relative increase of the number of resistant organisms present This is probably not due to stimulation of growth of resistant tubercle bacilli by streptomycin itself or to the development of dependent forms, but may result rather from the release of nutrient material in the

tuberculous tissue following the cessation of multiplication of the susceptible organisms so that the resistant ones multiply more rapidly in the absence of this competition

The net result is an increase in the resistant tubercle bacilli until the patient appears to be chiefly infected with this variety, in numbers as great if not greater than had been encountered before treatment started This not only precludes his obtaining any advantage from streptomycin treatment in the future, but makes possible the infection of other individuals by organisms which are already resistant to streptomycin so that they cannot later respond to this treatment This has actually been observed to occur If this were to be carried out consecutively it would mean eventually the complete futility of streptomycin treatment in almost all of the cases

Accordingly, the problem of patients in whom sputum conversion cannot be confidently expected to develop as a result of treatment, and particularly patients whose cooperation in preventing the spread of the disease to others or whose continuous institutional isolation following treatment cannot be relied upon, should be considered seriously before the administration of the treatment The prevention of such resistant forms furnishes the strongest argument for the brief courses of streptomycin now advocated, even though they may not prove to be quite as effective therapeutically as somewhat longer courses

Another consideration justifying rejection of the treatment would be in cases in which there is reason to expect that at a later date the treatment might be more important but where its efficacy might be impaired by premature development of resistance Thus, in patients in whom pulmonary resection, for example, is being contemplated, or in whom there is a lesion which might be expected to give rise to a fresh spread at a later time, the premature use of this treatment with the development of resistant forms may rob the patient of his chief chance for the successful management of such complication The possibility of intercurrent hematogenous miliary spread or meningitis, for which streptomycin is today the only known effective treatment, should also motivate against its use on light inconsequential grounds in those in whom residual resistant organisms might be expected to persist This also contraindicates the prophylactic use of streptomycin with thoracoplasty or other operation in which complications may be expected to be unlikely, since such use, even though it may occasionally result in the prevention of the complications only too often leads to the appearance of resistant organisms and thus loses for the patient the possibility of utilization of the treatment when it might be needed later

Cases have already been observed in which tubercle bacilli isolated before institution of streptomycin treatment already contained organ

isms resistant to the usual blood level produced by therapy In at least one instance this resulted from exposure of a previously uninfected worker to a patient already ineffectually treated with streptomycin, but resistant forms may occur even in the absence of such known exposure If such exposures are allowed to increase, it may become necessary in all cases to determine the streptomycin sensitivity of the bacilli before instituting this treatment In most cases at present, organisms are completely susceptible and beneficial therapeutic effect is to be expected The presence of a few moderately resistant organisms may still not interfere with apparent clinical response A few highly resistant organisms are apt to increase under treatment and so render the period of benefit short, while a preponderance of resistant organisms is apt to lead to initial failure of the treatment Even aside from the expenditure of money, material and time in the treatment and the jeopardizing of the patient by omission of other forms of treatment, and the possible toxicity of the drug, streptomycin may directly damage the patient harboring resistant organisms since it might stimulate the multiplication of these germs

Waksman and others have pointed out that if other agents, whether an antibiotic, a sulfone or other chemical, were found effective against the tubercle bacillus, their simultaneous administration would greatly lessen the danger of development of oragnisms resistant to either On the other hand, the consecutive employment of one agent after another does not hold out this promise Hinshaw has administered streptomycin, para-aminosalicylic acid and a sulfone, simultaneously, for this purpose, pointing out that their toxic effects are so different as not to be increasingly harmful to the patient on combination, while their therapeutic effect may be synergistic Even though this particular set of agents may not prove to be successful, other similar measures appear highly promising Several such partially effective agents are already known, though the hope for a new, single, highly potent, harmless but irresistible bactericidal agent against the tubercle bacillus is still unfulfilled Patients who previously develop predominantly resistant tubercle bacilli in their lesions may lose their opportunity to benefit from such adjuvant remedies

In the case of patients with a life expectancy of only a few weeks or months, this problematical possibility of a greater therapeutic regimen in the future may be irrelevant For those with a longer life expectancy, and particularly for the so-called "good chronic," it provides a compelling motive for eschewing the temporary symptomatic benefit to be derived from immediate streptomycin treatment now at the cost of developing resistant organisms which might preclude the much greater benefit expected from anticipated developments at a later date

SUMMARY

Streptomycin appears to inhibit multiplication of tubercle bacilli without killing them or interfering with several of their physiological functions Study of minimal lethal doses and of blood levels after varying doses in different species of animals and in individuals of different size and of the toxic consequences of various doses and blood levels have pointed out the limits of allowable dosage Animal experiments and clinical experience have established the minimal effective daily dose that may be given Smaller amounts given at greater intervals are safer and just as therapeutically valuable as the large amounts at frequent intervals which were earlier recommended The indications and contraindications for this treatment have become clearer but further developments in this field are confidently anticipated

MANAGEMENT OF NONTUBERCULOUS BRONCHOPULMONARY SUPPURATIONS

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BRONCHOPULMONARY suppurations of nontuberculous origin constitute a sizeable segment of long-term illness. The two conditions most frequently encountered, and which will be considered in the following pages, are suppurative bronchiectasis and lung abscess. The therapy suggested is that currently used by the authors in their hospital and private practice.

By way of introduction, it may be stated that the treatment of long-standing bronchopulmonary suppurations should not be influenced unduly by the fact that the disease affects chiefly the bronchi or the parenchyma. Lung abscess is often associated with bronchiectasis, bronchiectasis, with abscess formation. Indeed, one may be hard pressed to determine which preceded the other. Furthermore, treatment should not be influenced materially by the fact that the disease is or is not associated with foul smelling sputum, often referred to as "putrid" and "nonputrid" suppuration, respectively. In either case, the infection may or may not respond to simple measures and may or may not require surgery. As a result of bronchial obstruction, a putrid abscess may not reveal itself until relatively late in its course or only after it had penetrated the pleura. On the other hand, a bland bronchiectasis may, in time, become foul smelling as a result of secondary infection with anaerobic bacteria.

Finally, the treatment of bronchopulmonary suppurations cannot draw sharp distinctions between acute, subacute and chronic disease based on arbitrary time limits. Intensive penicillin treatment may convert an acute lung abscess into an indolent process in a few weeks and this may require major surgery to complete the cure. There are also occasions when a lung abscess of considerable duration may respond to

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measures which are usually effective only in the treatment of recent disease Furthermore, a seemingly recent infection may in reality represent an exacerbation of a preexisting disease of which the patient may have been unaware This applies particularly to bronchiectasis and, to a lesser extent, lung abscess These are a few reasons why one cannot depend on the time factor in determining types of treatment to be employed

In the final analysis, the proper management of bronchopulmonary suppurations rests on (1) the recognition of the etiologic agent or agents concerned, (2) precise localization of the disease, and (3) treatment directed toward (*a*) promotion of drainage of purulent secretions from the affected areas, (*b*) antimicrobial medication, (*c*) incisional or excisional surgery, as indicated, and (*d*) systemic support of the patient Effective treatment calls for timely and integrated use of medicinal, postural, antibiotic, bronchoscopic and surgical measures, one supplementing the other Present-day treatment of bronchopulmonary suppurations has no room for separate "medical," "bronchoscopic," and "surgical" compartments

SUPPURATIVE BRONCHIECTASIS

Bronchiectasis is a condition characterized by dilatation of the bronchi Although the lower lobes, especially the left lower, are most often involved, the condition may affect any portion of the lungs, including the upper lobes Among diseases of the chest, bronchiectasis is second in frequency to tuberculosis and often enters into the differential diagnosis of chronic pulmonary diseases, On rare occasion, bronchiectasis is caused by developmental defects Much more often the disease occurs as a result of changes in a lung following atypical and viral pneumonias, especially those complicating measles and whooping cough Influenzal pneumonia is a frequent precursor An unappreciated cause of bronchiectasis is extrabronchial compression by tuberculous lymph nodes A foreign body lodged in a bronchus may likewise give rise to the condition Bronchiectasis is often associated with bronchiogenic neoplasm, tuberculosis, chronic empyema and occasionally with diseases of the mediastinum, heart, esophagus and spine Obviously, the management of bronchiectasis depends greatly on whether or not the disease is "primary" or "secondary " For the present, we are concerned with the "primary" form

Bronchiectasis is a disease of youth Once established, it remains confined to the segment or segments of the lung initially involved Spill-over infection to uninvolved parts of the lungs may cause pneumonia but not bronchiectasis In the development of bronchiectasis, bronchial obstruction plays a decisive role Plugs of tenacious sputum in the small

bronchi, generated in the course of viral and interstitial pneumonias of childhood, cause atelectasis of the affected lung At first, there is enlargement of surrounding alveoli and dislocation of intrathoracic structures to compensate for the pulmonary collapse In time, the bronchi of the affected portion of the lung dilate in response to the constant negative pressure within the thorax resulting from the loss of lung volume The fact that bronchiectasis may, under certain conditions, be a reversible process, supports this hypothesis of "compensation" Some physicians stress the element of infection and its accompanying destruction and presumed weakening of the bronchial wall in the causation of bronchiectasis Although some degree of bronchial infection is almost invariably present, it is doubtful if it leads to bronchiectasis unless there is coexisting bronchial obstruction and atelectasis In any event, infection is the prime factor in the production of symptoms and in determining the type of treatment to be employed The bacterial flora is mixed and made up of Streptococcus viridans, Hemophilus influenzae, Diplococcus pneumoniae, Klebsiella pneumoniae and bacteria commonly found in the upper air passages

Diagnosis.—Depending on the extent and severity of the bronchial infection, one encounters relatively "dry" and "wet" forms of the disease Eventually most "dry" forms become "wet" It is important to keep this in mind in planning treatment What may seem a drastic measure may be conservative in the long run "Dry" bronchiectasis is associated with slight cough and expectoration, usually more pronounced during intercurrent seizures of respiratory infections Hemoptysis is frequent and characteristic of the condition Suppurative bronchiectasis is associated with cough, profuse expectoration of purulent, at times bloody or fetid sputum, fever, loss of weight and appetite, anemia and other systemic disturbances The course of the disease is punctuated by periodic exacerbations of symptoms especially during inclement weather When associated with fever, the disease behaves as an atypical, protracted pneumonia, in the relatively free intervals, as a chronic bronchitis

The signs elicited on physical exploration of the chest depend on the extent and location of the disease The most distinctive signs are obtained in young individuals with unilateral suppurative bronchiectasis, inconclusive signs, in older persons with bilateral disease associated with considerable fibrosis and emphysema One may obtain outward evidence of pulmonary shrinkage as indicated by displacement of the trachea and apex beat and retraction of the affected side of the chest On auscultation, there is increased vocal fremitus, tubular breath sounds, and rales The quality and quantity of the latter vary from one examination to another depending on the amount of secretion momentarily present in the bronchi A feature of suppurative bronchiectasis is an abundance of

auscultatory findings and a relative paucity of roentgenographic changes In tuberculosis, the reverse is true In the late stages of the disease, one often encounters clubbing of the fingers and toes, anemia, amyloidosis and other signs of bodily wasting

Roentgenographic examination of the chest of a patient with suppurative bronchiectasis is often deceptive as an indication of the extent and severity of the disease, but the markings are seldom within "normal" limits In the routine postero-anterior projection of the chest, there is usually accentuation of the hilar markings on the affected side One often sees parallel lines containing columns of air radiating to one or both bases When filled with iodized oil, these are found to be dilated bronchi Ring shadows may be demonstrable in the mid and lower lung fields, the puddled sputum in the rarefied areas simulating opacitis cast by iodized oil A characteristic finding is the presence of a triangular shadow at one of the bases, usually the right, indicative of an atelectatic bronchiectatic lobe A collapsed left lower lobe is apt to be retracted and hidden by the heart shadow

Localization.—The presence of bronchial dilatation can be established after adequate filling of the bronchi with radiopaque iodized oil Bronchography serves the equally important purpose of enabling precise localization of the disease It is beyond the scope of this paper to detail the technic of bronchography Suffice it to mention that about 20 cc of cold iodochlorol or lipiodol solution are required to map out the bronchi of each lung The bronchi should be emptied of secretion by postural drainage, if necessary by preliminary bronchoscopic suction, before the oil is instilled Each lung is preferably examined at a separate session, in order to obtain a clear visualization of all the segments Films are taken in the postero-anterior and lateral projections (Fig 138, *A* and *B*) Both lungs may be filled with oil simultaneously and films taken in the oblique projections Under such conditions there is some degree of overlapping of images One should not neglect to empty the lungs of iodized oil after the conclusion of the examination

The following are the positions assumed by the patient, with the help of the examiner or an assistant, in outlining the various bronchopulmonary segments To map out the right lower lobe, the patient sits upright leaning slightly to the right The angle should be greater when the left lower lobe is being filled After the instillation of the oil, the patient is made to lie on the face and then on the back to fill the anterior and posterior segments The middle lobe and lingular bronchi fill with oil when the patient is made to lie on the right and left side, respectively When the patient is made to lie flat, the chest at a lower level than that of the rest of the body, the oil gravitates to the upper lobe bronchi To insure filling of all the bronchi, the patient is gently rotated from side to side In

suspected bronchiectasis of the left lower lobe, it is essential that the lingular bronchi of the left upper lobe also be filled with oil For some unexplained reason, bronchiectasis often affects the lingula of the left upper lobe when the left lower lobe is involved Many unsuccessful results of resection of the left lower lobe can be traced to failure to excise a diseased lingula

The *treatment* of bronchiectasis will be considered later in conjunction with that of lung abscess

A B

Fig 138 —*Cystic bronchiectasis* A, Bronchogram reveals many small rarefactions in the right upper lobe filled with iodized oil, some showing fluid levels bronchi in the remainder of the right lung are uninvolved *B* Right lateral projection

LUNG ABSCESS

Lung abscess is a feature of suppurative pneumonia which has undergone cavity formation In the majority, abscess formation results either from necrosis of a pneumonia caused by pyogenic bacteria, or the sloughing out of a gangrenous putrefaction caused by anaerobic organisms In a small proportion, abscesses are caused by hematogenous implantations of infected emboli from distant foci or the breakdown of bland pulmonary infarcts Secondary infection following measles or influenzal pneumonia is an occasional cause of lung abscess Operative procedures in the oral cavity (tonsillectomy, adenoidectomy tooth extractions) as well as operations on other parts of the body, under general anesthesia are frequent causes of aspiration pneumonia leading to suppuration and abscess formation Temporary loss of consciousness during shock therapy coma, submersion and trauma may also lead to suppuration, likewise deep sleep following sedation or alcoholism Aspiration of a foreign body such as a peanut may give rise to lung abscess Suppurative pneumonia with ab

scess formation caused by aspiration of esophageal or gastric contents due to cardiospasm is not infrequent In brief, lung abscess finds a fertile field in individuals with poor mouth hygiene, pyorrhea and carious teeth in whom the cough reflex and cleansing mechanism of the air passages is interfered with or suppressed, allowing ingress of bacteria into the deep recesses of the lung

The bacteriology of lung abscesses has been a subject of detailed study by Smith In a series of 135 cases of primary pulmonary abscess, he found thirty-five which could be classified as pyogenic and 100, as fusospirochetal Abscesses caused by pyogenic bacteria are nonputrid, those caused by fusospirochetal and associated anaerobic organisms are putrid (malodorous) The former include Staphylococcus aureus, Streptococcus hemolyticus and the pneumococcal groups of organisms Putrid lung abscesses are caused by a combination of organisms which are predominantly anaerobic and which act in symbiosis Smith found that the minimum number necessary ot produce putrid lung abscess are one of the following types of spirochetes Treponema microdentium, T macrodentium, T vincenti, and T buccale, one of the two types of fusiform bacilli, small or large, a vibrio, and any one of several types of cocci

As mentioned previously, lung abscess is caused by aspiration of microorganisms into the lungs at a time when the normal protective mechanism of the organs is inoperative, as occurs following anesthesia, shock and the conditions mentioned previously As might be expected under such circumstances, an infected particle of pus or clotted blood is apt to gravitate and lodge in a posterior segment of a lobe, the individual being in the recumbent position This explains why the posterior segment of the right upper lobe, the apical segment of the right lower lobe and the posterior segments of the left lung are chiefly involved The more direct course of the bronchi in the right lung is responsible for the greater vulnerability of this organ to aspiration infection

The lodgement of an infected particle in the lumen of a bronchus causes atelectasis of the distal part and furnishes an anaerobic medium for the fusospirochetal group of organisms to grow in Inasmuch as the impaction is more likely to affect a small-sized bronchus, the disease almost invariably begins in the peripheral portion of a lobe The subpleural location of the lesion causes early pleuritis between adjoining lobes or between lung and chest or wherever the infected material happens to lodge Associated thrombosis of the lobular blood supply contributes to the rapidity of the parenchymal destruction The major part of the affected bronchopulmonary segment undergoes liquefaction, the contents being expelled eventually into one or more bronchi with the formation of a cavity

Pyogenic lung abscesses are often multiple and are more apt to be centrally located, the surrounding suppuration involving several bronchopulmonary segments In the late stages of the disease, there may be little to distinguish pathologically a pyogenic from a fusospirochetal lung abscess Advanced disease is associated with considerable degrees of fibrosis and bronchiectasis Empyema is quite frequent In addition to regional extension of the disease to the pericardium and mediastinum, metastatic deposits in the brain, spleen, liver and kidneys are not infrequent

Diagnosis —At times, the diagnosis of lung abscess is obvious from the history and symptoms alone, occasionally, the diagnosis is most difficult We have in mind a classical instance of a physician, aged 47, who late one evening had a tooth extracted, and shortly went to bed Ten days later, he developed a dry cough, a rawness in the sternal region and an offensive odor to the breath, but no fetid expectoration Roentgen examination of the chest at this time revealed a soft, irregular infiltration in the midportion of the left lung with an area of high light in the center (*Fig 139, A*) It was apparent that the patient had a beginning putrid lung abscess. He was admitted to a hospital where he received 80,000 units of penicillin every three hours and 40,000 units of aerosol penicillin three times a day After nineteen days of treatment, the infiltration cleared completely (*Fig 139, B*) The patient returned to his duties and has remained well since

A diagnostic problem was encountered in a woman, aged 34, who had cough and pain in the left upper chest and shoulder for about three months She had no sputum, hemoptysis or weight loss Roentgen examination of the chest revealed a circumscribed density in the left upper lobe (*Fig 140, A*) Tuberculosis was suspected but repeated examinations of the sputum failed to reveal acid fast organisms Furthermore, the pain in the chest was unusually severe and not in keeping with pulmonary tuberculosis The presence of a malignant neoplasm seemed hardly likely, especially since bronchoscopy failed to reveal any abnormality Although there was nothing suggestive in the history to make one suspect a suppurative lesion, it was decided to treat her for this condition The patient was admitted to a hospital where she received penicillin treatment intramuscularly and by aerosol, totaling approximately 1 million units a day After four weeks of treatment, the lesion in the left upper lobe cleared completely (Fig 140 *B*) Late in her hospital stay it was discovered that a year previously the patient had received shock treatment for a depressive state a fact which she had kept hidden A routine roentgenogram of the chest preceding the shock treatment was within normal limits Close questioning revealed the additional information that the husband had noticed in the past year an offensive breath from

A

B

Fig 139 —*Pulmonary suppuration, ten days after a tooth extraction* *A*, Soft infiltration in left upper lobe with several areas suggestive of rarefaction *B*, Absorption of infiltration after nineteen days of penicillin treatment (80,000 units, intramuscularly, every three hours, and 40,000 units by inhalation, three times a day) Well and at work a year later

A

B

Fig 140 —*Lung abscess following shock treatment* *A*, Circumscribed density in left upper lobe, scattered infiltrations with a round transluscent area immediately below *B*, Absorption of density and infiltrations after four weeks of postural, bronchoscopic and penicillin treatment (approximately 1,000,000 units a day by injection and inhalation) Has remained well

his wife Obviously, we were dealing with a putrid lung abscess of possibly one year's duration which responded surprisingly well to penicillin therapy

There are many occasions when a patient fails to disclose important facts which would be helpful in diagnosis One who had been on an alcoholic spree, or one who had been knocked unconscious in a fight, is very apt to keep such information from the physician However in most instances once can elicit a history of a previous operation or a period of loss of consciousness In such, the appearance of cough, fever, hemoptysis, expectoration of fetid or non-fetid sputum, depending on the nature of the infection, and the occurrence of localized pain in the chest are highly suggestive of lung abscess, provided, of course, the roentgen findings are in keeping It should be emphasized that in the presence of poor oral hygiene, fusospirochetal and anaerobic organisms are plentiful in the mouth so that aspiration infection can occur spontaneously during sleep and at other times

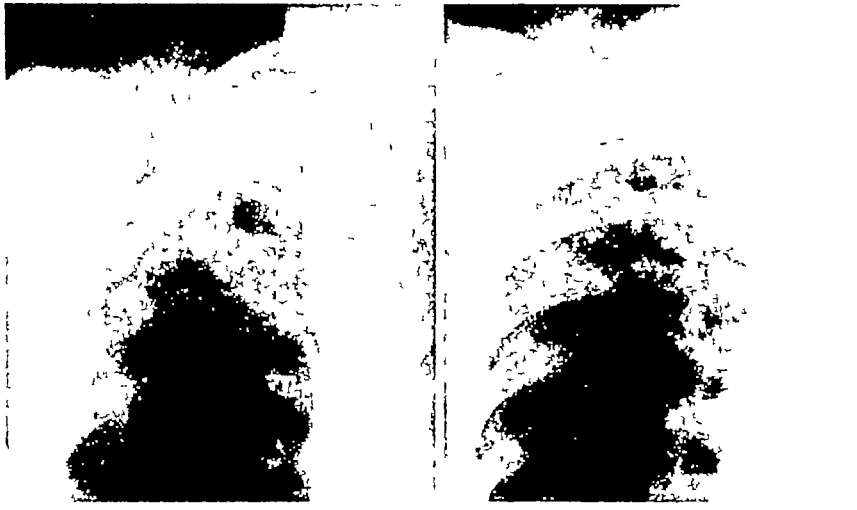
Some of the roentgen features of lung abscess are exemplified in the films illustrating this paper At the onset of the disease, the roentgenogram is apt to reveal an ill-defined density in the mid-third of a lung In a short time, one or more areas of high light may be discernible in the central part and, shortly thereafter, a single cavity showing a fluid line at the lower pole (Fig 141, *A*, *B*) The fluid line is often the most conspicuous part of the abscess and serves to direct attention to the existence of the antrum which might otherwise be overlooked At times, the roentgenogram fails to show a distinct cavity In such, an overexposed film may be revealing

An important step in the diagnosis of lung abscess is bronchoscopy It should be done at least once in every patient suspected of having the disease and may be used in selected cases as part of the therapeutic regimen It may be possible to localize the abscess by the smell emanating from the affected part of the lung The appearance of the draining bronchus may also be informative In addition, bronchoscopy may disclose a foreign body or neoplasm as the underlying cause

Localization — Exact localization of the disease is a prerequisite not only as a preoperative measure but for nonsurgical treatment as well The patient may be able to indicate with his finger the site of the abscess inasmuch as localized pain is a feature of the disease when the parietal pleura is involved The roentgen examination should include lateral as well as postero anterior projections Sectional films, in addition to revealing the abscess cavity which may not be demonstrable otherwise allow estimation of the distance the abscess is from the chest wall, occasionally the draining bronchus leading into the abscess may also be seen

TREATMENT

The treatment of bronchopulmonary suppurations is governed by the following objectives the institution of adequate drainage, disinfection, and eradication of diseased parts The desirable agent or combination of agents, the appropriate antibacterial medication and whatever else the therapeutic regimen may entail depend on what one expects to accomplish and the facilities available During a long illness, there may be occasions when the patient will require treatment at home, in the physician's office or in a hospital In one case, the indication for treatment may be a threatening or actual flare-up in the course of a chronic disease In



A B

Fig 141 —*Lung abscess in an alcoholic of 62 A,* Density in right upper lobe with a large cavity showing a fluid level *B,* Resolution of process with disappearance of cavity, after six weeks of postural, bronchoscopic and penicillin treatment (100,000 units, intramuscularly, every 3 hours and 100,000 units by inhalation three times a day) Striking clinical improvement, normal temperature on fifth day of treatment with rapid disappearance of foul smelling sputum

another, one may be dealing with an acute process which one hopes to cure without an operation In still another, the treatment may aim to prepare a patient for surgery Obviously, one has to be guided by broad principles rather than rigid formulas

The current emphasis on antibacterial medication has served to relegate to the background the less dramatic forms of treatment of the disease Physicians have much to learn from surgeons who place great weight on measures which aim to improve a patient's nutrition before an operation No less can be done for an individual who is not fortunate to meet surgical requirements Every effort should be made to build up the

patient's strength with a high caloric, high vitamin diet, including a liberal intake of easily digestible proteins Acute lung abscess is often associated with emetic cough in which case it may be advisable to withhold mouth feeding for several days and to administer intravenously protein hydrolysate with dextrose Blood transfusions are especially useful In the presence of anoxia, oxygen should be given Drug medication may include iodides, ephedrine and codeine Barbiturates may be given but not in amounts to suppress free expectoration If the disease is associated with wheezing respiration or other signs of bronchial obstruction, inhalations of vaponefrin are helpful The vaponefrin is administered *immediately preceding inhalations of antibiotic*

The treatment of acute lung abscess should be intensive and maintained The response to treatment is reflected in the patient's symptoms, vital signs and the appearance of comparative roentgenograms The latter determine whether or not to continue therapy along the same lines or to apply other measures In the treatment of a lung abscess, especially the putrid variety, complete eradication of the disease is essential *inasmuch as a smoldering focus may light up later and require major surgery* As mentioned elsewhere, bronchoscopy should be done at least once in every instance of pulmonary suppuration We are in full agreement with Samson to the effect that patients are rarely too sick to be subjected to bronchoscopy, rather, "they are too ill not to be bronchoscoped" An acute lung abscess is an emergency and the only place to treat the patient is a hospital where the services of a thoracic team are available

The efficacy of antibacterial medication of bronchopulmonary suppuration is unpredictable At times the results are most gratifying (Fig 142, *A*, *B*), at other times, disappointing In assessing the value of an antibiotic one should not lose sight of the fact that the sensitivity of bacteria varies widely among different species and even within members of the same species It stands to reason that the clinical response can reflect only the degree of sensitivity of the dominant group of organisms Under ideal conditions, it is desirable before starting treatment to identify the strain of organisms and to test its sensitivity to penicillin and streptomycin In practice, however, reliable bacteriologic information is not often available One is, therefore, forced to assess the efficacy of a particular line of treatment by the results

Inasmuch as bacterial resistance to an antibiotic rises rapidly if the dose is sublethal or is maintained for a long time the agent should be administered *in maximum concentrations even if the condition does not* seem to warrant intensive medication Acute pulmonary suppurations of recent onset require at least a million units of penicillin a day applied through one avenue or another As to the relative indications of penicillin and streptomycin in the treatment of bronchopulmonary suppurations,

it is customary to initiate the treatment with penicillin because the infective flora of the respiratory tract is usually gram-positive Streptomycin is applied if the infective flora is predominantly gram-negative Prolonged penicillin administration often sees a conversion of the flora

A B

Fig 142 —*Suppurative pneumonia with multiple abscesses in a diabetic man of 60 A,* Right upper lobe shows massive consolidation with a number of transluscent areas and one large area of rarefaction at the lower aspect *B,* Absorption of the process with residual thickening of the interlobar fissure. During a period of three months, patient received postural, bronchoscopic and penicillin treatment (600,000 units penicillin in oil, intramuscularly, daily, and 100,000 units, orally, three times a day) Striking improvement with gain of 30 pounds in weight, resumed factory work

from gram-positive to gram-negative organisms Streptomycin should, therefore, be used if there is a lag in the clinical response to the treatment Although combined penicillin and streptomycin appears to possess additive effects, it is inadvisable to use up all of one's ammunition at once in the treatment of bronchopulmonary suppuration As mentioned previously, careful bacteriologic examinations are of utmost importance.

To simplify discussion, the several modalities of treatment will be taken up individually

Drainage —The evacuation of purulent secretions from the affected parts of the lungs is the keystone in the treatment of bronchopulmonary suppurations In the case of bronchiectasis, this may be accomplished by postural evacuation, if necessary supplemented by bronchoscopic aspirations In the case of lung abscess, thoracotomy and drainage may be necessary because of the subpleural location of the disease and the fact that the draining bronchi are small and often obstructed However in many instances of lung abscess bronchoscopic removal of inspissated secretions improves internal drainage This procedure warrants a short trial in conjunction with postural and antimicrobial medication In the initial stages of the disease bronchoscopy is primarily a diagnostic procedure

The proper application of postural drainage takes into consideration the site of the disease, the slope of the draining bronchi, the age, physical condition and cooperativeness of the patient Upper lobe bronchiectasis drains best with the patient in the upright (Fowler s) position The relatively dry, odorless character of upper lobe bronchiectasis is due to the facile drainage from this part of the lung Midzonal disease drains best with the patient in the supine position, the diseased side uppermost Since midzonal bronchiectasis, involving the right middle lobe or the lingula of the left upper lobe, is usually associated with lower lobe disease, the most productive position is one with the patient lying flat the foot of the bed raised about a foot above the floor Frequent changes in position help to dislodge the secretions, which are then coughed up more easily Lower lobe bronchiectasis requires the patient to bend over the side of the bed at the hips, the elbows resting on a low cushioned stool which supports a catch basin The patient is urged to cough and expectorate in this position An intelligent patient quickly learns the best position to assume in order to empty the lungs with the least effort

Short periods of postural drainage ten to fifteen minutes at a time, every three or four hours serve to cleanse the main channels but not the secondary radicles which are the ones usually involved in bronchiectasis To evacuate the latter, continuous drainage is necessary for hours at a stretch Although continuous drainage is possible by proper positioning it is more comfortable to use specially constructed beds which allow multiple positioning Homemade appliances can often be used as a makeshift Obviously individuals requiring prolonged drainage fall into a group for which surgical treatment is not feasible because of advanced age poor physical state or other reasons

Antimicrobial Treatment —Sulfadiazine in 1 gm doses given every three or four hours, for several days is helpful in the treatment of pu

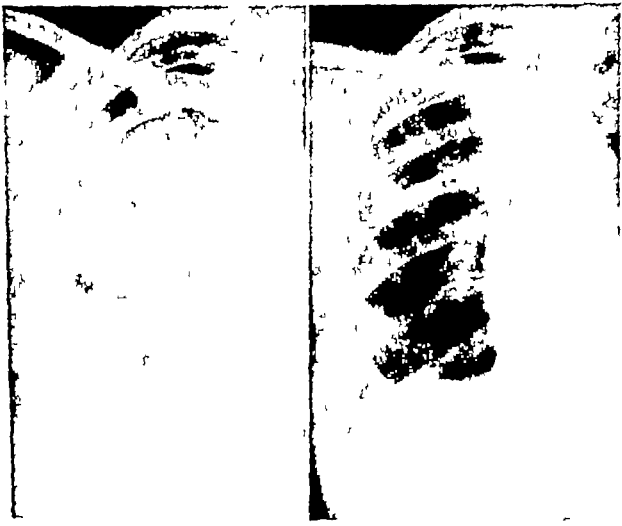
tients with bronchiectasis at the inception of upper respiratory infections which are apt to cause flare-ups of the disease Currently, we are prescribing for patients inhalations of micropowdered penicillin dust in doses of 50,000 to 100,000 units two or three times a day This method of applying antibiotics directly to the respiratory tract, originally proposed by Taplin and Bryan, promises to supplant oxygen pressure tanks and other expensive and cumbersome apparatus used for the administration of aerosol vapors Investigations by Krasno, Karp and Rhoads indicate that this method is more effective than aerosol vapors because of the more protracted absorption of the antibiotic as indicated by the effective serum levels obtainable as late as three to three and one-half hours after inhalation

If the infection persists for more than forty-eight or seventy-two hours and is associated with fever and increased expectoration, an injection of 300,000 units of procaine crystalline penicillin G is indicated It is repeated daily until the acute episode subsides A less desirable substitute is the administration of oral penicillin tablets in doses of 100,000 units, at three hour intervals By judicious use of sulfadiazine, alone or in combination with penicillin, it is often possible to abort or cut short an acute respiratory infection which might otherwise cause a prolonged exacerbation of a chronic pulmonary suppuraion

Once the infection gets a foothold and there is a return of excessive cough, purulent expectoration and fever, more intensive measures are called for We find it helpful to anesthetize the upper air passages, larynx and trachea with about 5 cc. of 2 per cent butyn, as in the performance of bronchography, and to instill by means of a curved cannula 100,000 units of penicillin dissolved in 5 cc of water directly into the larynx and trachea The thorough toileting of the bronchi which follows slow cocainization of the throat and larynx serves a most useful purpose This procedure may be repeated several mornings, in the office, at which time an intramuscular injection of 300,000 units of penicillin is also given At home, the patient inhales 100,000 units of micropowdered penicillin several times a day Preceding each inhalation of penicillin, the patient empties the bronchi of accumulated secretion by postural drainage A supplementary bronchoscopic suction may be necessary A week or ten days of this type of treatment usually brings to termination an acute flare-up in the course of a chronic pulmonary suppuration

Antimicrobial treatment of acute lung abscess requires large doses of penicillin, preferably combined with sulfadiazine and, if the response is not satisfactory, streptomycin In the presence of hyperpyrexia, it may be well to initiate the treatment with an intravenous effusion containing 1 million units of crystalline penicillin G This is followed by intramuscular injections of 100,000 units every three hours, day and night (Fig

143, 4, *B*) As a substitute, 600,000 units of procaine penicillin G may be administered intramuscularly every twelve hours As soon as the acute symptoms subside, the dose can be cut to 300,000 units twice a day Although it is doubtful if much inhaled penicillin enters the affected bronchopulmonary segments, there is much to recommend the inclusion



A B

Fig 143 – Suppurative pneumonia with multiple abscesses in an alcoholic of 40 A, The major part of the right lung is occupied by dense infiltrations with a large cavity showing a fluid level at the base and several smaller ones above it *B* Three months later, there is resolution of the pneumonia and disappearance of cavities Received postural treatment sulfadiazine (2 gm three times a day for one month) and penicillin (100 000 units intramuscularly, every three hours and 50 000 units by inhalation four times a day for eleven weeks) Striking clinical improvement with decline in temperature from a range of 101 105 F to normal in two weeks foul smelling sputum disappeared at the end of a month Discharged to Morrisania City Hospital Chest Clinic for follow up examinations

of topical applications of the antibiotic as soon as free drainage is established By inhalation 100 000 units of micropowdered penicillin are administered two or three times a day

Sulfadiazine is given by mouth three or four gm as an initial dose followed by 1 gm every four hours Streptomycin is given intramuscularly in 0 3 gm (500 000 units) doses every twelve hours The particular

type of medication used and the dosage are governed by the nature of the disease and the course of events Penicillin should be continued until there is complete cure of the disease, a period which takes in surgical treatment if found necessary

It is beyond the scope of this discussion to detail the possible side reactions accompanying sulfadiazine and antibiotic medication The physician should be thoroughly familiar with their manifestations and the means of their prevention and treatment

Surgical Treatment.—The conditions which may call for surgical intervention in the management of bronchopulmonary suppurations are (1) lung abscesses which fail to respond to medical treatment, (2) bronchiectasis in suitable cases, and (3) complications resulting from the aforementioned, especially those involving the pleura, mediastinum and chest wall

1 A lung abscess of recent origin which does not improve rapidly with postural, bronchoscopic and antimicrobial medication requires surgical treatment, unless there are contraindications to the use of the latter The surgery utilized may be thoracotomy and drainage, or resection Surgical drainage is indicated in instances of single abscesses associated with copious amounts of sputum which do not respond to medical treatment The efficacy of the latter is usually evident within two or three weeks The past few years have witnessed a decided reduction in the number of patients requiring open drainage, owing to the early and intensive use of antibiotics and ancillary measures By the time the surgeon sees the patient, one is likely to be dealing with a subacute or chronic abscess requiring extirpation rather than drainage (Fig 144, *A*, *B*, *C*, *D*) All too often, if the latter is attempted in a patient who has had prolonged penicillin treatment, a chronic granuloma is encountered and little, if any, free-flowing pus

As emphasized previously, if surgical drainage is contemplated, accurate localization of the abscess by means of multiple positioning roentgenography and tomography is a prerequisite With the patient in the upright position, to prevent flooding of the tracheobronchial tree and under local anesthesia to preserve the patient's cough reflex, the abscess is approached through the periosteal bed of the overlying rib Following resection of the selected rib, the position of the abscess is confirmed by needle aspiration before it is entered The abscess is then incised, loculations broken and the cavity packed with gauze Later, rubber tubes are inserted These are removed after closure of the bronchopleural fistula by which time only a narrow sinus tract usually remains Healing is permitted by slow obliteration of the abscess cavity from below up

Lobectomy or pneumonectomy, depending on the nature and extent of the disease, as well as on what the surgeon finds on opening the chest,

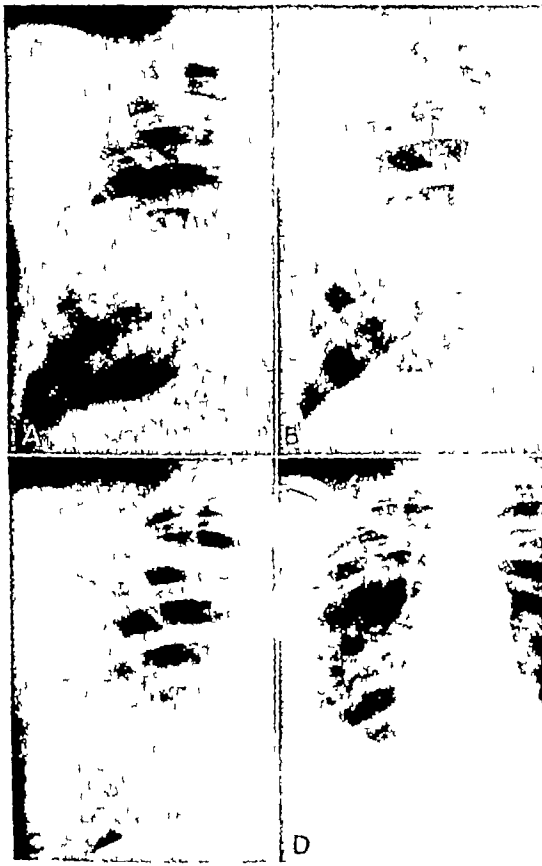


Fig. 111.—*Lung abscess in alcoholic patient of 47. Thoracotomy and lobectomy unsuccessful. Lobectomy.* A. Irregular density occupying middle of right lung with irregular area of rarefaction in center. *B.* Slight reduction in size of mass after one month of postural drainage and penicillin treatment (50,000 units intramuscularly every three hours and 50,000 units by inhalation, three times a day). After one month of treatment patient left hospital without consent. *C.* Readmitted two months later at which time all symptoms and signs were due to residual disease. X-ray reveals cavity (left, upper) lobe. *D.* Thoracotomy successful. Resection of right lower lobe performed. Patient well at first visit [illegible]

are the procedures of choice in the treatment of subacute and chronic lung abscess Ample time should be allowed to prepare the patient for operation in the manner outlined in the preceding pages An unobstructed tracheobronchial tree, an afebrile disease and a patient in good physical state spell the difference between an uneventful and a stormy postoperative course Resecting a chronic lung abscess carries a higher morbidity and mortality than does resecting a lung which is the seat of bronchiectasis Patients with chronic lung abscess are generally older and have sustained considerable pulmonary damage Resecting a lung abscess may be more prolonged as a result of dense pleural adhesions and induration around hilar vessels

2 The medical treatment of bronchiectasis is, at best, palliative If successful, the patient's cough and expectoration are greatly reduced but the cleansing and disinfection do not restore the dilated bronchi to a healthy state A new infection may nullify the labor of months The treatment of choice is resection of the involved bronchopulmonary segments In properly selected and well prepared cases, resection offers an individual a chance for complete cure and carries a low mortality rate (Fig 145, *A*, *B*, *C*, *D*) It is possible to treat surgically bilateral bronchiectasis by staged resections of the involved segments providing there is adequate respiratory reserve The operation of pulmonary resection for bronchiectasis has become well standardized and has been developed to a point where uninvolved portions of the lobes need not be sacrificed

Surgical treatment of bronchiectasis may be advised as soon as the disease is diagnosed and the extent of involvement ascertained bronchographically The lungs should be free of iodized oil before the operation Failure to make them so may lead to a stormy postoperative course and incomplete reexpansion of the nonresected portion Young persons with unilateral disease are the best candidates for resection The operation is an elective one permitting adequate preparation of the patient and optimum timing of the operation In addition to the study of pulmonary function, due regard must be given to the cardiorenal status, especially in older patients The preoperative preparation should include measures to improve the nutrition of the patient with repeated blood transfusions and a high protein, high vitamin diet, in addition to local treatment to the lungs, as outlined in the previous pages Repeated bronchoscopic aspiration is often highly effective in the preparation of patients for resection It is a good policy to have a chest roentgenogram taken within twenty-four hours of the operation to disclose any last minute changes in the pulmonary condition In the immediate postoperative period, the patient is watched for signs of retention of bronchial secretions He is encouraged to cough, if necessary, one resorts to intratracheal aspiration by means of a rubber catheter Early ambulation is desirable

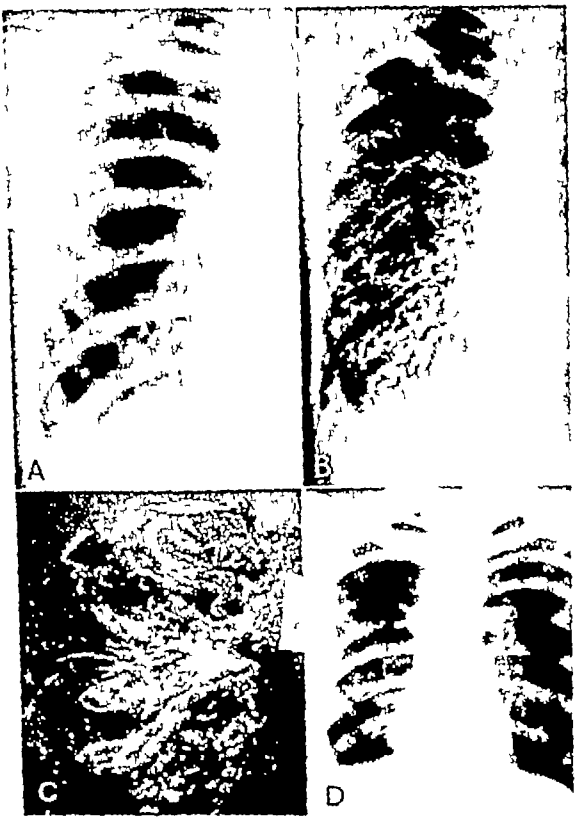


Fig. 145.—*Suppurative bronchiectasis in a boy of 11. Lobectomy.* *A*, Triangular density at base of right lung showing columns of air; obliteration of right costophrenic sinus. *B*, Bronchogram reveals dilated bronchi in the basal segments of the right lower lobe. *C*, After postural and penicillin treatment, resection of diseased area. Specimen reveals dilated bronchi in fibrotic lung. *D*, Two months after operation, complete reexpansion of non-resected lung. Beginning bone healing of cut ends of resected 6th and transected 7th ribs. Gain of 11 pounds. No cough or expectoration, returned to school.

9. A discussion of the treatment of pleural and other complications of bronchopulmonary suppurations is beyond the scope of this paper. Their management is largely in the domain of the surgeon.

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NEW TRENDS IN THE TREATMENT OF BRONCHIAL ASTHMA

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An asthmatic attack can be interpreted as a defense reaction designed to ward off antigens to which sensitivity exists, and which are about to enter the system. It can be likened to an inflammatory process which localizes and neutralizes harmful bacteria. In asthma this process takes place mainly in the bronchi. The secretion of mucus tends to dilute and eliminate the antigen, the cough reflex assists in its elimination, the attraction of eosinophils and other leukocytes aids in rendering the antigen innocuous, and emphysema present in asthma tends to close up the interalveolar stomata and thus prevent further absorption of antigens into the blood stream. This defense mechanism is lacking in incipient asthma, especially in infants and young children[1] who do not readily develop these clinical features. Instead, manifestations of anaphylactic shock and death, formerly called "thymic death"[2] ensue. Here we observe lymphocytosis, hyperplasia of lymphoid glands, petechial hemorrhages and allergic edema in the lungs followed by secondary pneumonitis. The presence of edema in other organs suggests that the antigen or its harmful products have entered the system.

The defense reaction of an asthmatic attack is associated with certain morbid changes which are largely produced by histamine and similar substances formed as a result of the antibody antigen reaction. These changes account for the symptomatology of asthma. Partial obstruction of bronchi by bronchospasm and by mucus, stimulated by histamine, induces the characteristic wheezing similar to musical sounds heard in partially obstructed tubes of wood and brass instruments. This is accompanied by dyspnea, anoxia, cough, restlessness, dehydration, malnutrition, and, often, by signs of secondary infection. Treatment must be directed towards the control of these symptoms and simultaneously toward interfering as little as possible with the various protective functions of the system.

Four different situations present themselves, each of which calls for different therapeutic action. These are (1) the emergency, (2) the chronic asthmatic state, (3) the state of rehabilitation and (4) the complications.

THE EMERGENCY

Emergencies arise from inhalation, ingestion or injection of antigens to which extreme sensitivity exists. Bronchospasm and bronchial edema

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[1] Emergencies in young children and infants will be discussed later.

with or without urticaria on skin and mucous membranes[3] characterize this condition One of the most common sources of allergic shock in adults is ingestion of aspirin Ingestion of any food, particularly of fish, nuts or cottonseed, inhalation of animal hair or dusts of organic and non-organic chemicals, or therapeutic injections of any biological may lead to allergic shock, if the patient exhibits excessive sensitivity to the product This condition is also encountered during skin testing and in treatment with antigenic extracts Here, its most serious aspect is the accidental puncture of veins, and the intravenous injection of a potent antigen

Effective relief and, indeed, the patient's life, depends on the promptness with which treatment is administered Further details on allergic shock from pollen injections are presented in Table 1

In order to prevent emergencies from intradermal testing, the following rules were set down elsewhere[4] 1 In young children and infants who are most susceptible to severe reactions, no intradermal skin tests should be performed Instead, testing should be done by the passive transfer method on a nonallergic recipient on sites which had been injected two days previously with 0 1 cc of the patient's blood serum 2 No tests should be given for antigens to which a history of a severe reaction from inhalation or ingestion had been obtained If hyposensitization with such an antigen is desirable, a high dilution (e g , 1 100,000) should be made for the initial dose 3 In proceeding with intradermal testing, an attempt should be made to gauge the patient's skin reactivity by testing for those antigens first from which generalized reactions are uncommon, such as fungi and fruits If these initial tests indicate marked sensitivity, testing material for more potent extracts should be diluted, especially those for fish, nuts, legumes, melons, animal danders and cottonseed * 4 Superficial veins should be avoided Arms and legs are preferable to the back as sites for the tests because a tourniquet can be applied in case of a reaction

THE CHRONIC ASTHMATIC STATE

In treating chronic asthma the following facts should be borne in mind (1) Chronic perennial asthma is usually initiated at, or shortly after the termination of the pollen seasons[5] (Fig 146) The attacks are likely to become aggravated at subsequent pollen peaks It is the constant, uninterrupted absorption of an antigen (pollen, house dust, fungi) rather than the occasional one that accounts for chronicity in asthma (2) Food is a minor factor in chronic asthma In only five (10 per cent) out of fifty-six cases did complete disregard of food sensitivity aggravate the asthmatic state [6] (3) Cessation of symptoms following ad-

* Preliminary dermal testing is no definite safeguard against general reactions

TABLE I

ANAPHYLACTIC SHOCK FROM POLLEN INJECTIONS*

	Manifestations		Time of Appearance	Mechanism	Treatment	Prophylaxis
	Local	General				
[illegible]	[illegible]	[illegible]	From 10 to 90 minutes. Proportionate to size of overdose and degree of severity	Wrong judgment. Large fresh extract. Simultaneous absorption of antigens from previous injection, from ingested foods to which latent sensitivity exists, from inhalants especially spores in air	Tourniquet above site of injection. Epinephrine (0.05 to 0.2 cc.) repeated if necessary. Aminophylline intravenously (0.25 gm.) for dyspnea.	Cautious labelling of vial. (Careful gauging patient's sensitivity to consider simultaneously absorbed antigens). With fresh extract reduce dose. Watch patient for 15 minutes after injection
Dark passages	Pain from [illegible] to [illegible] from [illegible] extract in presence of local [illegible] swelling rapidly	Above more acute and severe. Moderate degree of shock	1 to 10 minutes	Accidental puncture of vein followed by back seepage of extract into vein	Tourniquet. 0.5 cc. to 1 cc. epinephrine. Intravenous aminophylline or antihistaminics (50 to 50 mg.)	1. Avoidance of visible veins 2. Withdrawal of plunger for evidence of blood before injection. 3. Watch for blood on area of injection 4. Tight pressure on injected area if blood appears 5. Always keep epinephrine and other drugs ready
Accidental intravenous	Pain from area from patient is asleep	Above extreme. Immediately when a cutaneous stress not recognized	Within 10 to 15 seconds	Intravenous injection	Above. Larger doses may be required. In extreme state 0.1 cc. of 1:1000 epinephrine intravenously with 10 cc. of with drawn blood injected very slowly (Larger doses may lead to cerebral and cardiac damage)	

* The reader who is called treatment pertains to shock from any other antigen

† Disturbance of local [illegible] and [illegible] pain (temperature, [illegible] pain, vomiting, convulsions, etc.)

ministration of a certain measure does not indicate that this measure is responsible for the so-called "cure" since with the disappearance of certain pollen or fungi from the air and the spontaneous termination of intercurrent respiratory infections, the allergic balance tends to become reestablished (4) Prolonged use of any drug is liable to aggravate asthma, its discontinuance may lead to the patient's improvement (5) By our efforts to reduce the patient's untoward symptoms, we may interfere

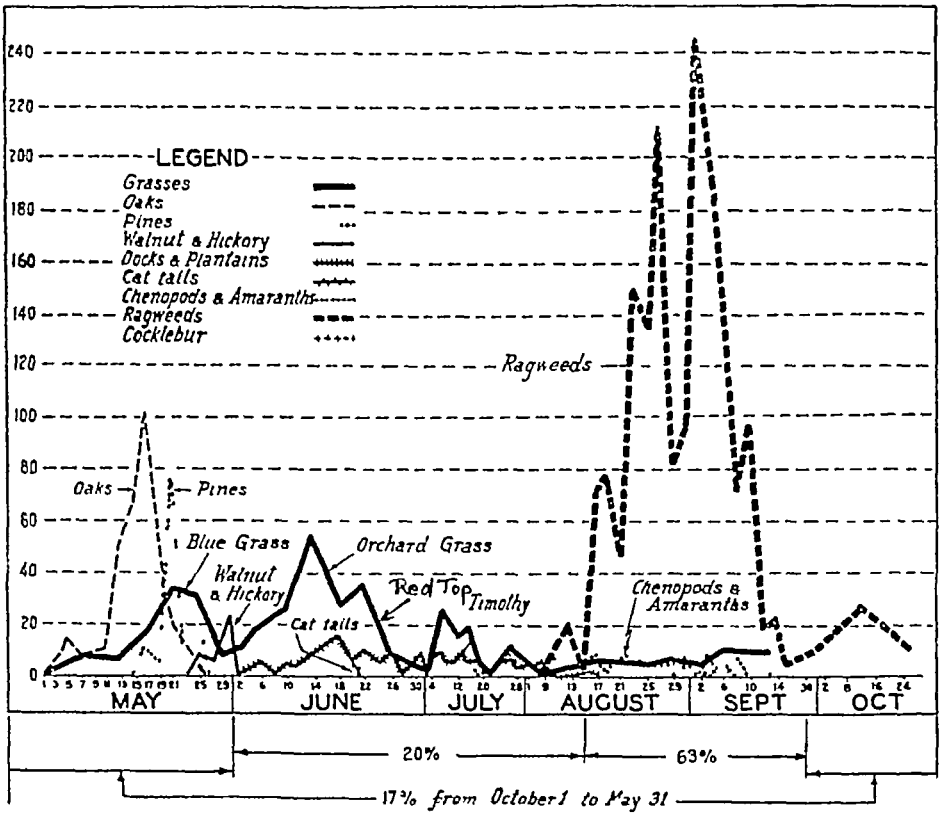

Fig 146 —This is a differential pollen count of Detroit (1929) The percentage figures below indicate the dates of onset of asthma in sixty-five patients The first attack of asthma occurs at the height of the ragweed season in the highest percentage of patients

with the natural tendency to recovery Furthermore, practically all drugs in use for asthma are conspicuous by their unpleasant side effect Drugs should, therefore, be employed with great discrimination

In chronic asthma, the following are our therapeutic aims (1) to improve the patient's immunological balance, (2) to aid the system in eliminating damaging antigens, (3) to counteract the effect of the antigen-antibody reaction, histamine, and (4) to render symptomatic relief

Improvement of Immunological Balance —This can be accomplished

by (*a*) preventing contact with damaging antigens, (*b*) hyposensitization (building up protective antibodies), (*c*) control of infection

Avoidance of Harmful Antigens.—In a patient with chronic asthma avoidance of such extraneous agents as dust, animal hair, flowers and feathers is essential. His removal to a "clean" hospital room from his home, to the dust of which he may have been conditioned, may bring about cessation of the attacks.* Certain therapeutic measures should be discontinued which had been in use for some time, particularly otherwise harmless medications. The worst offender in this respect is epinephrine when used habitually by spray or by hypodermic injections. Once a patient is given a hypodermic syringe or an atomizer, it is difficult to break him of the habit of reaching for it at the slightest apparent need. If one recalls the appearance of those who use epinephrine habitually, their striking pallor, tremor and constant tachycardia, one cannot help but feel that the withdrawal of this drug constitutes a major therapeutic step. The same is true to a lesser extent of ephedrine and drugs related to it. There is the added chance that sensitization to ephedrine may be established by its frequent use, both through oral and topical administration.

Opiates should not be employed in asthma. They diminish the cough reflex and thus further the tendency toward asphyxiation. I have encountered serious ill effects from every narcotic available, including pantopon and demerol which I formerly considered harmless. Another extremely dangerous drug often habitually used by asthmatics is aspirin. It frequently relieves asthmatic attacks, which accounts for its favor with patients as well as with makers of patent asthma remedies. I have had occasion to review the records of several cases of sudden death from aspirin. When asthmatic seizures are extremely severe, the possibility that the patient had taken this drug should always be borne in mind.

Short Interval Hyposensitization.—The most striking and yet most neglected means of relief for chronic asthma is rapid hyposensitization with the seasonal pollen or with other inhalants to which the patient gives strongly positive skin reactions. It is based on the common observation that a patient with hay fever will obtain most out relief during the hay fever season following one or several injections of extract of the causative pollen provided the dose is large enough to produce a local wheal of moderate size and not too large to cause an aggravation. In selecting the pollen and fungi I am guided by the results of my surveys of pollen [illegible] in Figures 116 and 117. In winter

* [illegible] the patient [illegible]

house dust, fungi and greatly diluted bacterial antigens are employed in conjunction with antibiotic therapy

TECHNIC —The initial dose is determined as follows If a preliminary scratch test is strongly positive, no injection is given until the wheal produced by the test has subsided * An initial intradermal injection with 1/10 of a unit to 3 units of the pollen extract is then administered If the

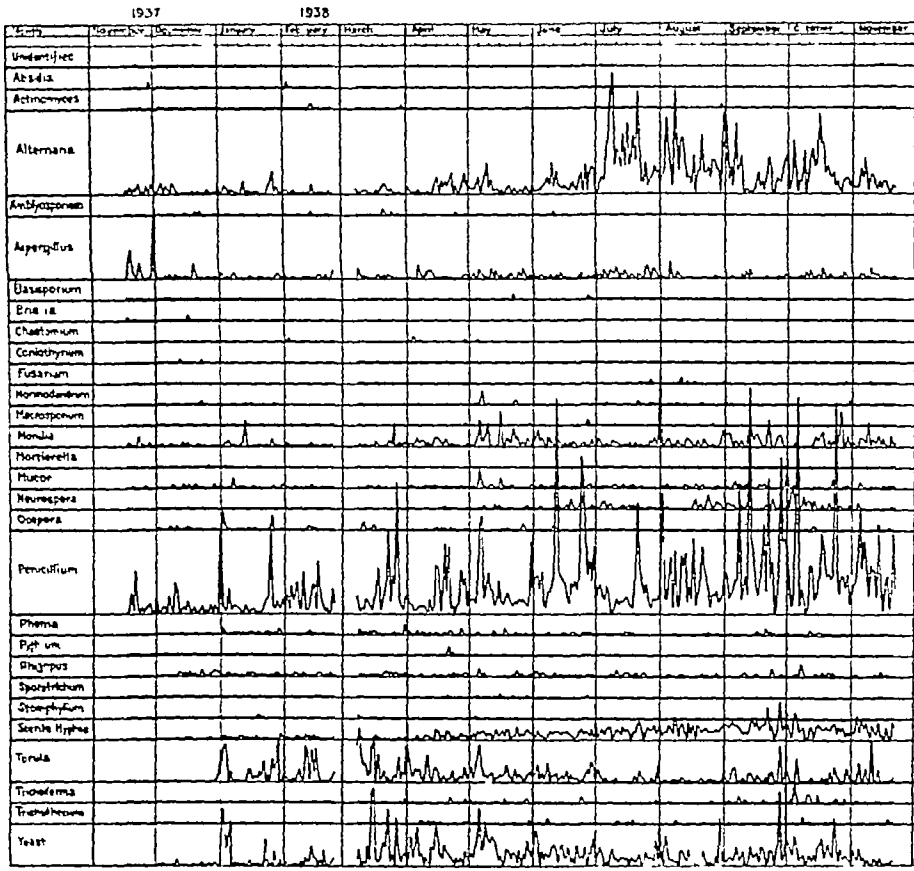

Fig 147 —This chart represents the results of determination of fungus spores in the air obtained by means of daily exposures throughout one year There are minor fungus peaks throughout the year Alternaria shows a definite seasonal tendency in late summer and fall, torula and yeast in the early part of the year Penicillium is the most prevalent fungus throughout the year Asthmatics tend to become worse on days of fungus peaks (From Waldbott, G L, Ackley, A B and Blair, K E J Lab & Clin Med, Vol 26)

scratch test had been negative doses from 10 to 30 units are chosen These doses are increased at intervals of fifteen to twenty minutes until a dose is reached which produces a good-sized local wheal From then on, the size of

* Repeated skin testing (production of wheals) occasionally accomplishes a hyposensitizing effect

further injections is gauged cautiously and the intervals between injections lengthened in such a manner that the effect of the previous injection has subsided before another is administered. If the doses are properly gauged, the asthmatic attacks begin to clear up simultaneously with the development of a wheal, as dramatically as from an injection of epinephrine. If improvement does not ensue, either too much or not enough pollen extract has been given or antigens other than the ones chosen for treatment may be dominant in the production of the asthma. Constant watch should be kept to prevent an overdose as indicated by an excessive local wheal at the site of the injection and by aggravation of the asthmatic attack by the treatment. The injections should then be discontinued for several hours or even days until the flare up is controlled.

Control of Infection.—Control of infection is now considered a major step in the treatment of chronic asthma regardless of whether the disease originated from an intercurrent upper respiratory infection or whether infection is superimposed upon primary allergic sensitivity. Sulfa drugs (0.5 gm. every four hours for two to three days) and, preferably, penicillin and streptomycin, should be chosen according to the clinical manifestations. Personally, I prefer penicillin administered intramuscularly every three hours to the inhalation method and to the procaine penicillin injections. Intradermal skin tests for penicillin must be given before each course of treatment. Serious accidents (allergic shock) from sensitivity to penicillin acquired through a previous course have been observed. Leukocytosis, purulent sputum, an increased sedimentation rate and the presence of a low grade temperature are indications for this treatment. For control of infection in the sinuses, sinus lavage is rarely required. Sinus surgery may be useful only if extensive polypoid degeneration of the mucosa and other secondary structural changes are present which did not improve with antibiotic therapy.

Elimination of Antigen from Lungs.—Therapy directed toward elimination of antigenic substances from the lungs embraces bronchial catharsis and relief of bronchospasm. The latter releases mucus for expectoration.

In observing a patient with severe asthma it is obvious that wheezing and cough tend to subside the moment a quantity of mucus is expectorated. Expectorant drugs, particularly potassium iodide, ammonium chloride and special* intravenous injections of sodium iodide (10 per

* [illegible]

[illegible] 10.0 gm. (7 [illegible])
[illegible] 18.0 cc. (5 [illegible])
[illegible] q.s. 100 cc. (5 [illegible])

[illegible]

cent aqueous solution), aid in this process The two drugs of choice for relief of bronchospasm are aminophylline and epinephrine Rarely is there any need to employ doses larger than 0 1 to 0 2 cc of epinephrine Doses of this size are as effective as larger ones and much less harmful Small doses of the aqueous solution are far preferable to epinephrine in oil or gelatin The slow rate of absorption of such preparations renders their therapeutic action more uncertain, interferes with antigenic treatment and prolongs the unpleasant side effects of epinephrine In employing aminophylline intravenously, doses of 3 to 5 cc of the 10 cc ampule ($3\frac{3}{4}$ grains) injected slowly are sufficient to control attacks of average severity Aminophylline is the most effective and least unpleasant drug employed in asthma It can be given as an enema, in suppositories, or intramuscularly in doses of $7\frac{1}{2}$ grains, or orally (enteric coated!) in $1\frac{1}{2}$ or 3 grain doses Other bronchodilators such as ephedrine and the new products Isuprel and Amphaphrene are useful additions, but less desirable than aminophylline because of their unpleasant side effects The latter two drugs are best administered by aerosol inhalation (1 200) Time-honored asthma powders containing stramonium and iodide, or asthma cigarettes are of definite value in certain cases * Occasionally an injection of caffeine sodium benzoate (0 5 gm) secures considerable relief of bronchospasm

Clinicians agree that death in asthma is due to obstruction of bronchi by thick, gluelike mucus It acts as a check valve similar to a foreign body in the bronchi Its removal by bronchoscopic lavage, therefore, should be considered as obligatory a procedure as the removal of a foreign body from the bronchi or a tracheotomy in diphtheria Even if the patient presents a poor surgical risk, this operation should be performed In eight cases[8] this measure has been life-saving Of 152 therapeutic bronchoscopies on 112 additional patients with chronic asthma, cessation of attacks was secured in fifty The success of this treatment depends entirely on whether or not the characteristic mucus is present in the bronchi It is of little avail in cases in which the clinical picture is dominated by bronchospasm, namely, in asthma of psychosomatic origin and in incipient allergic asthma, where urticaria-like edema and little mucus is found [1] Certain precautions should be observed[8] directed toward prevention of accidents which principally result from sensitization to, or intolerance of, local and general anesthetics and other medications employed during bronchoscopy

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* R

Powdered Stramonium Leaves	1 0 gm (15 grains)
Potassium Nitrate	1 3 gm (20 grains)

Sig Ignite small portion of powder and inhale fumes

Measures to Counteract Histamine.—We are now able to counteract the harmful effect of the antigen-antibody reaction by drugs which neutralize histamine and histamine like substances. There is a definite place for these drugs in the treatment of asthma. They relieve bronchospasm and aid in drying up the bronchial secretion. They relieve the nightly cough which is so annoying to patients and control minor attacks. In combination with other drugs, especially aminophylline (Hydrollin, Searle), they are said to be more effective than either drug alone. Given intravenously (20 to 50 mg.) they relieve attacks of moderate severity. Because of their soporific action they are not as desirable as aminophylline or epinephrine. They are contraindicated in dehydrated patients when the bronchial mucosa has become dry, as they inhibit further mucus secretion and thus counteract bronchial catharsis.

Symptomatic Measures.—Symptomatic therapy in asthma is concerned with securing rest, relieving cough, establishing proper nutrition, counteracting dehydration and controlling anoxia.

Considering that the slightest exertion aggravates asthma, the need for complete relaxation is generally appreciated. The best position for an asthmatic is propped up in bed, his head leaning on a food tray on which a rubber covered pillow is placed. Because sensitization to and particularly intolerance of, certain hypnotics may exist, only one or two sedatives are preferable to a large variety. My preference is chloral hydrate in retention enemas of 1 gm., enema consisting of equal parts of ether in oil (2 to 3 ounces each), phenobarbital orally or hypodermically. For anoxia, mixtures of oxygen and carbon dioxide (90-10) or of helium and oxygen (79-21) are occasionally required. Sometimes, however, this measure increases the patient's discomfort and anxiety, particularly when—as is often the case—no noticeable cyanosis is present.

For the maintenance of nutrition, intravenous administration of glucose (25 per cent) and vitamins B and C (after preliminary intradermal skin test) are useful. Sudden loss of weight from dehydration should be counteracted by large doses of fluids, glucose (10 per cent) and amino acids. In an experience of more than 500 transfusions of blood plasma or whole blood given to asthmatics, I have observed startling effects on several occasions. Although it is difficult to present proof, there are indications that through blood of certain individuals, protecting β blocking γ antibodies can be transmitted. Caution should be exercised in selecting blood for transfusion, since harmful reagins may also be transferred. We employ a preliminary skin test (0.1 cc. intradermally) with several prospective blood specimens and choose the one which produces the smallest wheal or flare. Allaying the patient's fears and

worries as well as that of his surroundings plays a significant part in supportive therapy *

REHABILITATION

After subsidence of asthmatic attacks, an important phase of treatment begins which necessitates a reversal of many measures carried out during attacks

Nutrition —Our first concern is the improvement of the patient's nutritional state Immediately after an asthmatic attack, foods which previously had been harmful can usually be eaten with impunity An attempt should be made to disregard former food sensitivity and to employ high caloric diets Only those foods are eliminated which are definitely recognized as harmful Others from which the patient had refrained before are gradually and cautiously added to the diet Only rarely is it necessary to eliminate food for a long time It is much more difficult to combat the patient's fears of eating a certain food than to overcome the sensitivity to the food

Inhalants —An effort should be made to adjust the patient to normal surroundings in order that he will learn to overcome sudden exposure to "overdoses" of inhalant antigens There is ample evidence that asthmatics absorbing an antigen repeatedly at short intervals suffer much less than if this antigen is avoided strictly and happens to be accidentally inhaled, ingested or injected Furthermore, by trying to impose too many restrictions on the patient, we succeed in isolating him psychologically from his surroundings and provoke most serious inferiority complexes While general cleanliness in a house is stressed, elaborate dust precautions as the disposal of upholstered furniture, rugs and household pets which may have been harmful before should not be carried out if it has been ascertained that these antigens do not induce attacks

Effort.—An important phase in rehabilitating the patient is the improvement of his threshold of tolerance to effort As soon as possible he

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* NOTE I have used an unconventional method of treatment which is being widely publicized by lay people, namely that of Dr Gay of Biloxi Mississippi This is a prescription consisting of the following

℞

Fowler's Solution	6 0 cc (ʒ iss)
Potassium Iodide	6 5 gm (ʒ iss)
Tincture of Digitalis	2 33 cc. (35 minims)
Saccharin	0 065 gm (gr i)
Elixir of Phenobarbital	q s 120 cc (℥ iv)

Its content is basically the same as that of most patent medicines This medication is likely to produce remarkable improvement under thoroughly controlled conditions The danger of arsenic poisoning through large doses should be kept in mind

is to initiate light exercise several times a day, such as walking, climbing stairs, bending, squatting, at first with moderation and indeed with caution. This program is intensified if he remains free from attacks. Even such activities as playing golf, bicycle riding, climbing, hiking and swimming—things which are otherwise harmful to the patient—*should* be encouraged at this stage. If not tolerated, they should be discontinued for a few days or weeks. Here, too, the boost of the patient's morale by insisting on having him perform normal activities which had heretofore been forbidden, universally outweighs any temporary ill effect.

Cold Sensitivity.—The principle of gradually building up a tolerance is further utilized as follows. Most asthmatics are sensitive to sudden temperature changes. Some develop severe attacks when exposed to sudden temperature changes, especially to cold. Duke's advice to build up a resistance to cold has been a distinct adjunct to our treatment. It consists of gradually exposing the skin to cold water through sponging arms and legs at first and later through rubbing ice on the body surface. Some patients thus acquire the habit of taking a cold bath daily and are consequently conditioned to brave the winter months.

Climate.—To recommend a change of climate to a patient is frequently a convenient means by which a doctor rids himself of a patient with whom his treatment has failed. Caution should be employed in making this recommendation. The patient often considers the act of breaking up his home and moving to a different climate his last resort. If this experiment fails, despondency and despair ensues. A thorough investigation of the fungus and pollen situation of the prospective territory should precede any such recommendation and should be carefully checked with the patient's sensitivity. Moving the patient to the house next door may have the same effect as sending him far away. It is particularly harmful to have patients return from a pollen free area at the height of the pollen season. This frequently elicits the first attack of asthma.

Psychosomatic Factors.—It is not difficult to appreciate why the psychosomatic element plays such an important part in asthma. Some of the chief factors which make for a psychosomatic aggravation of asthma are the patient's fear of attacks, his concern about becoming asphyxiated, his habitual use of harmful medications, his insecurity in his earning ability and his inadequacy in his role as husband and father. Through the many slights which have been imposed upon him throughout his life by doctors, relatives and friends he has become psychologically isolated from his surroundings. Worried relatives, especially mothers in the case of children, contribute further to his insecurity. In overall effectiveness the physician may at times contribute toward

TABLE 2

SYMPTOMS AND TREATMENT OF COMPLICATIONS OF ASTHMA

Complication	Chief Manifestations	Treatment
From Mucous Plugs		
Atelectasis—lobar	Shock, pain in chest, shift of mediastinum	Bronchoscopic aspiration and lavage
Atelectasis—lobular	Localized wheezing, impairment and compensatory emphysema	
Bronchiectasis	Persistent expectoration of purulent mucus, rales in lower portions of lungs	Bronchoscopic aspiration, antibiotics, surgery, if confined to pulmonary segments
Bronchostenosis	Persistent localized wheezing, sudden febrile episodes	Bronchoscopic dilatation
From Cough		
Subcutaneous emphysema	Localized swelling	Conservative, incision
Mediastinal emphysema	Crepitation, pressure on trachea	Aspiration of air, relief of cough
Spontaneous pneumothorax	Absence of breath sounds, shift of mediastinum	None
Cystic degeneration of lungs	Extreme emphysema, persistent wheezing	None
Spontaneous rib fractures	Pain on inspiration and on palpation of ribs	Immobilize chest
From Anoxia		
Convulsions (in children)		Avoid antihistaminics
Syncope (in adults)	Extreme cyanosis, seizures last ½ to 1 min	Spontaneous recovery
From Other Sources		
Pneumonitis	Localized wheezing, rales, fever, leukocytosis, consolidation, if extensive	Antihistaminics at onset, antibiotics
Lymphoid hyperplasia	Increased dyspnea	Irradiation of hilum glands

aggravating this situation as in asthma. Conversely, a physician may completely alleviate asthma of long standing through encouragement, proper counsel concerning the various aspects of the disease and through teaching the patient and his family an intelligent approach to the above problems. It is rarely necessary to refer him to a psychiatrist for lengthy — and costly — treatments.

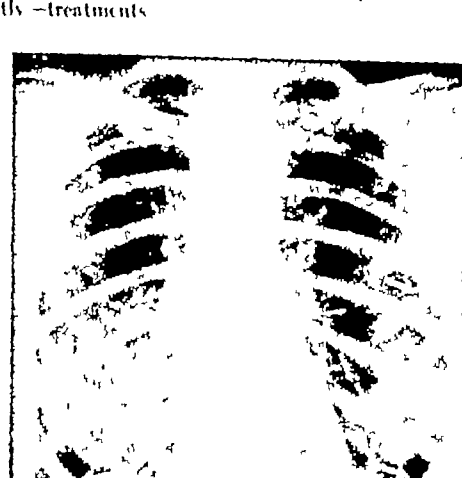

FIG. 18. Spontaneous rib fractures in a case of chronic allergic asthma.

COMPLICATIONS

Most complications of bronchial asthma (Table 2) are due to (1) obstruction of bronchi by mucous plugs, (2) excessive cough and (3) anoxia.

Sequelae of mucous obstruction are atelectasis (a portion of the lungs or of whole lobes) and bronchiectasis. Accumulation of mucus in the terminal bronchi and subsequent infection may lead to bronchiectasis. Permanent bronchiectasis as a sequelae of allergic asthma is much less common than is said from the literature. On the other hand a certain degree of bronchiectasis probably exists in most

chronic asthma and subsides upon the termination of the attack Bronchograms indicative of such lesions taken during an asthmatic attack were negative when repeated after its subsidence

Persistent and severe cough may induce such rare conditions as subcutaneous emphysema, mediastinal emphysema, spontaneous pneumothorax and cystic degeneration of the lungs Spontaneous rib fractures, a complication from severe coughing (first described by Waldbott[10]) may account for severe chest pain (Fig 148)

Children occasionally exhibit convulsions during attacks associated with marked anoxia The equivalent of this condition in adults may be sudden syncope occurring during severe coughing spells The patient falls on the floor, remains unconscious from one-half to one minute, his face being markedly cyanotic Spontaneous recovery occurs promptly with the disappearance of cyanosis

Hyperplasia of hilum glands may enhance the state of dyspnea through pressure on bronchi, especially in children Here, x-ray treatment over the hilum glands is most effective and results in much benefit This is similar to the effect from radium treatment of hyperplastic adenoids which aids in the permanent recovery from asthma

The most common complication of asthma is localized pneumonitis This is sometimes mistakenly diagnosed as virus pneumonia, especially in incipient asthma, where it may initiate the disease Here it represents an allergic edema in the lungs which is followed by secondary infection Another mode of origin of pneumonitis in asthma is secondary infection of localized atelectatic and bronchiectatic areas

SUMMARY

In the treatment of asthma, four different phases present themselves, each of which requires a different mode of approach These phases are (1) the emergency, (2) the chronic asthmatic state, (3) the state of rehabilitation, and (4) the complications

An effort should be made not only to counteract the morbid changes and symptomatology of the disease, but also to assist the system in its natural defense, both during the attack and after its subsidence

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CHRONIC ILLNESS AND THE CONSTITUTIONALLY INADEQUATE

A Rational Approach to Treatment

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CAUSES OF CHRONIC ILLNESS

THE first question is, what are the most likely causes of chronic, long-term illness? In my experience, the most important factor is a poor nervous inheritance, which causes the patient to feel tired and "peglegs" off and on all his life. Usually, if one takes a careful history, one can find that other members of the family were nervous wrecks, too, or perhaps alcoholic or even "a bit off." Many persons feel well and strong all their days and never want to go near a physician, but these chronic invalids never feel well, and they are always going to doctors or taking medicine. They have to force themselves to work. Most of them have many aches and pains throughout the body, most of which are probably projected out from the brain. Many of them have symptoms which are due to their autonomic nerves playing tricks with a normal heart, digestive tract, uterus, urinary organs or skin. Many of these persons are subject to sick headaches or to headaches of other types. Many are overly sensitive or lacking in stoicism, hence every little annoyance or discomfort becomes magnified into an ache or a pain. Many of them have a poor resistance to infection, hence they are often down with bad colds from which they recover slowly.

Many of these people can best be described as "constitutional inadequates"; they were born frail with a poor nervous system, and they are unable to stand up well to the strains of life. Any extra burden tends to knock them out. Perhaps, largely because it is so hard for them to go on working and earning a living, any little accident or illness is likely to be used as an excuse for not working or for not standing up to face the world.

Many "chronics" easily develop puzzling symptoms of hysteria. Some of them are shy, reticent individuals who do not adjust well to life. It is very hard for them to meet people. Others are mildly manic-depressive, and in their depressed spells they develop many aches and pains and indigestions which are thought to be due to disease in some abdominal organ.

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Many of the chronic complainers have a decided tendency toward arthritis or fibrositis, and this accounts for much of their complaining and disability Others appear to have poor materials built into their cardiovascular-renal system They have palpitations, a poor "wind," cold clammy hands, and bluish, cyanotic legs They don't stand up well to work or to anything else

A large group of chronic invalids are primarily pathologic worriers, they are constantly being scared to death with the idea that they are very ill or that they have cancer and are going to die Hence they are always running to physicians to be reassured Some are so afraid of illness that they prefer to have the abdomen explored again and again, trusting in this way to avoid disaster Other "chronics" are primarily hypochondriacs, the worst of whom are mildly insane on the one subject of health They are the people who feel so strongly that some organ is diseased that it is impossible to talk them out of it Often they act as if they didn't want to be reassured

In older persons there are a number of special causes of chronic illness, such as emphysema or a tendency toward asthma, severe arthritis, hypertension or cerebral arteriosclerosis with little strokes

Many of the "chronics," when seen by a physician, have a "nervous breakdown " They cannot work and see people Often the break came mainly because of poor nervous heredity, but in other cases it followed severe strain or illness or an accident or overwork Usually, in the worst cases in which one breakdown after another occurs, the patient has a poor nervous heredity and is mildly manic-depressive The nervous breakdowns which come out of a clear sky are the worst, those that are due to overwork are generally soon cleared up if the patient can get a vacation or some rest

WHAT TO DO BEFORE TREATMENT IS STARTED

Obviously, before a physician starts treating a person with a long story of illnesses, he should try to get a good idea as to the diagnosis Too much of the treatment being given today to "chronics" is inefficient, futile and unsuccessful because it is misdirected The physician starts treating before he knows what the real trouble is He doesn't realize that he is dealing with a chronic invalid who never can be made over into a well person by any operation or by any form of treatment Oftentimes he doesn't even suspect the fact that the patient's main trouble is a neurosis or a mild psychosis, with perhaps a depression Few physicians today realize how many of the patients who go through their hands each month are mildly insane or nervously handicapped "relatives of the insane "

Obviously, the first thing to do is to make as good a diagnosis as possible. A good examination is always helpful and should be made, but I doubt if these examinations need be repeated again and again as today they so frequently are. So often the attending physician or consulting internist would not want to repeat the examination if he were only to sit down long enough to take a good history, to size up the patient, and to recognize the type of person the patient is.

Often, after a few questions, one can say to a patient, "Primarily your autonomic nerves are playing tricks on you, and the reason they are doing this is because they are poorly balanced. They are poorly balanced probably because, as you just told me, your grandfather and uncle are in the insane asylum. This instability of your autonomic nervous system is your share of the family curse. The curse that injured your ancestor's brain appears to have injured your sympathetic nerves. You need not go on fearing that you will go insane, because you already have your inheritance, but you will probably often suffer to some extent from nervousness."

To another patient one can say, "Your troubles appear to be due mainly to your tendency toward fibrositis and arthritis. Ever since you were a child you have had pains in various joints, you have had attacks of wry neck, cricks in your back, lumbago, sacroiliac trouble, and aches through your thoracic and abdominal walls." To another person one can say, "Your digestive tract is weak or perhaps too sensitive, or there is a strong tendency for the waves to run back over your stomach and up your gullet, carrying gastric juice into the back of your throat and causing 'acid stomach,' easy regurgitation or heartburn."

NO SIMPLE REMOVABLE FOCUS RESPONSIBLE FOR THE WHOLE ILLNESS

Perhaps the worst thing that we physicians do to chronic invalids today is to try to find one focus of disease somewhere in the body which when removed will leave the patient well. Usually, the patient and his family are highly desirous of a most thorough examination, one that will reveal this imagined focus. For years they keep going from one physician or clinic to another, hoping that someone will be so thorough that he will find the cause of the illness. They spend all of the family's money following this will-o' the wisp. The saddest feature is that consultants usually agree with them and search interminably for the focus.

Actually, in my experience, such examinations of chronic invalids rarely bring forth any spectacular results. They result mainly in a waste of time and money. Often any good internist could tell the patient the first day that there was little sense in examining him.

A SEARCH FOR THE CAUSES OF "FEVER"

A certain number of chronic invalids keep going to consultants to find the cause of a low-grade "fever" (99 6°F) in the afternoons Usually, this is thought to be due to brucellosis, and the blood agglutinates the Brucella organism in low dilutions Generally, this must be disregarded In practically all of these cases the rise in temperature does not represent fever and is not due to infection The temperature is normal or it is up a little because of the patient's nervousness and tension No other cause can ever be found for it, and the patient never comes to any bad end because of it Rarely can a sane consultant confirm the diagnosis of brucellosis Even if he were to confirm it, the diagnosis couldn't possibly explain why the patient has been ill most of his life, long before the so-called fever appeared

TREATMENTS TO AVOID

One of the most important things to avoid in handling patients with chronic troubles is the useless operation As every physician knows, so many persons with chronic disorders—especially if there is distress in the abdominal region—talk themselves into a number of operations which do no good The appendix is removed, perhaps then an ovary or tube, perhaps then the uterus and perhaps later the gallbladder Then there may be one or two operations for adhesions, perhaps a kidney is anchored, perhaps part of the thyroid gland is removed, perhaps the coccyx is removed, and perhaps a breast is removed because of some cysts Usually the result of all this work is nil, and the patient is, if anything, worse than before

WHAT CAN BE DONE IN THE WAY OF TREATMENT

In most cases the best thing one can do is to get the chronic invalid to see what the real trouble is and why it can never be completely eradicated Many of these persons are immensely helped by being told what is their real trouble They must be made to see that the little abnormalities found by other physicians and considered responsible for their troubles are only minor variations from normal which have no deep significance and cannot possibly explain their illness Then, if they have the intelligence and grit to accept this view, to adjust their lives to their handicap and to learn to live within their means of strength, they can be much better If we physicians can get them to stop looking for one cause for all their troubles, and a cause which can be cut out, we will have done a great deal for them Often I say to a frail, constitutionally inadequate and ailing woman, "The next time you feel like spending $200

for an examination, spend it on a high school girl who can help you with your dishes after dinner, that will do you much more good."

In many cases the best medicine or the only one that could do any good for a frail, sickly person would be an annuity of $3,000 a year, but obviously this is out of the question.

Explaining Away Previous Diagnoses Made Elsewhere.—One cannot help chronic invalids and one cannot get them to see the essential problem until one explains away tactfully the diagnoses that have been made elsewhere. So long as a jittery, half insane woman thinks all her troubles are due to a low blood sugar, a low blood calcium, "an acidic condition of the system," anemia, a low basal metabolic rate, coloptosis, a spastic colon or diverticulosis, she cannot be helped.

Often, all that is needed is to repeat several times the test that was supposed to reveal disease. Then it will become obvious that the home doctor's laboratory technician was in error. In other cases, perhaps the blood sugar or the blood calcium or the basal metabolic rate was a little low, but then the patient must be shown that it was within limits of normal. Perhaps, also, the patient can be reminded that his home physician for months filled him with calcium or thyroid substance without doing him any good, and this, again, shows that the laboratory report was wrong.

When the patient is much concerned about some ptosis of the abdominal organs he must be shown that this is normal. Spasm in the descending colon is to be expected in all tense persons. An older person who is much worried over colonic diverticula must be shown that they are found in a high percentage of healthy oldsters, and that in all but a very few cases they are harmless. Many a chronic invalid has been scared half to death over an electrocardiogram which was said to show myocardial infarction but was really normal for the person's age. Many hours in my working week are spent in telling persons either that I cannot find the little abnormality which was found at home, or else that I cannot look on it as a sign of disease. To me it is only a harmless variant from normal. Sometimes I have to point out that even a gallstone in the patient's case is not producing symptoms; it couldn't possibly explain all the patient's miseries, and its removal can do no good.

Teaching the Patient to Live with His Frailness.—As I have already said, one of the most important things we physicians can do for the chronic patient is to teach him to live within his means of strength. So many persons are always fretting and fussing and worrying and wasting the strength which they so greatly need. Many have to be taught to go to bed earlier or to take some medicine to help them sleep. Some men and women have to try to get into a better job, one which is within their

means of strength Sometimes, under exhortation from the physician, a patient, either male or female, will make some change or adjustment which will make life much more bearable and easy and healthy I often tell patients of the refined, educated man whom I found in the mountains of western Montana running a gas station I asked him what he was doing there, and he said that he had had one of the finest law practices in New York but he couldn't stand the gaff After every appearance in court he was ill, and so he finally gave up and went west to take an easy job The income was barely enough for his needs, but he was well and in two years had had neither a headache nor a stomach ache It would be wonderful if more constitutionally frail persons could make such an adjustment to life!

There are many unhappy women who owe much of their chronic illness to their dissatisfaction with their marriage Some of these women are much better when they either leave the husband and strike out for themselves, or else face the fact that they will never bring themselves to get a divorce Then they can settle down to make a better go of their marriage

The Harmlessness of Many Myomas of the Uterus —One of the worst things which we physicians now do to women with chronic illness is to remove the uterus because it contains one or two small myomas Oftentimes even a large one had better be left, especially when it isn't producing flooding and it hasn't lowered the hemoglobin content of the blood It seems wrong to take out such a uterus when the operation almost certainly will not change the health of the woman, and may throw her into a depression or a very disturbing and long-lasting menopause Many physicians say, "But the lesion may become malignant " If it does, it will obviously have to turn into a sarcoma, and sarcomas of the uterus are rare In forty years of practice I have seen very few The longer I practice and the more sense I get, the fewer myomas I have removed So far I have not had to regret leaving in even a fairly large myoma, and I have seen hundreds of women whose nerves and lives were wrecked by a hysterectomy

Medical Treatment —As one would expect, there are no wonderful drugs which will suddenly cure people with chronic troubles and constitutional frailness The family physician just has to keep meeting emergencies as they arise, and he has to make the patient as comfortable as he can, often with the help of sedatives I haven't any faith in the relaxant drugs, such as belladonna I doubt if they do what they are supposed to do As troubles come along, the family physician must treat them colds, infections, sprains, headaches, backaches, arthritis, insomnia and indigestion Always, if he is wise, he will keep in mind that he is not curing the patient but only tiding him over

The medicines which I use most often for chronics are barbiturates to

help them sleep at night If a person has been lying awake night after night and I can get him to sleep well, I am most likely to get him rested and back to a fair degree of health Where there is no sleep there is not much chance of recovery For those many persons who wake around four in the morning and cannot get to sleep again, I give bromural, which is a short-acting sedative It will let the patient waken at seven with his mind clear I do not like giving phenobarbital every day or several times a day, as many physicians do Especially if the patient already feels somewhat depressed this seems to me a poor treatment Sometimes, if the patient is jittery during the day, I will give a tablet of bromural Ordinary bromides in large doses are bad because they are not excreted fast enough and sometimes they produce a mild intoxication and psychosis

Occasionally, when a person is depressed, a tablet of desoxyn or benzedrine may help a bit, much as would a big cup of black coffee

For those many persons who have aches and pains everywhere due to fibrositis, I often prescribe a hot bath, and if the patient can get it and afford it, baking and massage

For persons with a chronic tendency toward indigestion and no findings to indicate organic disease anywhere in the digestive tract, I sometimes try a smooth diet More often, if there is any suggestion of food sensitiveness, I give the patient instructions to keep a record of unusual foods eaten, so that perhaps he can learn which foods regularly cause him distress Many chronic 'dyspeptics' have what I call the 'small laboratory disease' By that I mean that they cannot digest a large meal of any kind They can get along fairly well if they live on small meals of simple foods, simply prepared

For those many persons with psychosomatic aches and fibrositic pains in the thorax or abdominal wall I give reassurance, and often prescribe a certain amount of stoicism Often these people are much better when they become convinced that their ache is not due to serious disease and is not going to 'turn into anything,' such as a cancer or an ulcer

For those many bright faced, keen little women whose headaches and great tendency toward fatigue and chronic illness are due to migraine, I prescribe a more restful life with, if possible, a nap in the afternoon They must get sufficient sleep, and they must try not to be such perfectionists When they get a headache or a badly upset stomach, they can usually be greatly helped by the immediate hypodermic injection of gynergen or of D H E 45 In bad spells they may be helped by a rectal suppository containing nembutal

For those many persons with hypertension I haven't much medicine to offer Many can be helped most by reassurance It helps many to know that there are four types of hypertension, the first two mild and fairly

harmless and the last two severe and dangerous It then is a great comfort to a man to know that his disease is of type 1 Hypertensives who are too stout often can be much helped with a reduction diet As they lose weight, the pressure often comes down Such persons often will be better, also, if they live more quietly There are a few cases in which a lumbar sympathectomy is indicated and will help The operation should not be done if the patient is over 45 and the pressure does not come down with rest or after the taking of certain drugs A few patients may be helped by taking potassium thiocyanate, but this is a drug that can do harm Most persons with hypertension do not need medicine A simpler life often constitutes the best treatment

Many of the neurotics and psychoneurotics can be greatly helped by reassurance, by mental purgation, and by efforts toward a better adjustment to life and their particular problems. Many of these persons do well if they have a kindly physician to whom they can occasionally go for advice and reassurance They need sympathy and understanding and friendly care Above all, they need to be kept out of the hands of certain specialists and surgeons who are likely to do too many things to them The physician who, during the course of thirty years, keeps a psychopathic woman from having six or seven abdominal operations has done a splendid job

The patients with the worst psychic difficulties should be induced to place themselves in the hands of a sensible psychiatrist That is where they belong

MASTERY OF LONG-TERM ILLNESS

JURGEN RUESCH, M.D.*

ADAPTATION to long term illness taxes to the utmost the physical and psychological resources of an individual. While in acute disease the patient finds himself suddenly removed from his environment and habitual field of activity, he can after a varying length of time usually continue where he left off. In contrast, long-term illness changes the mode of living itself. Psychologically speaking, ideals, goals, beliefs, attitudes, interests, social techniques and daily habits have to be modified, while physically speaking the body has to find reparative and compensatory mechanisms for management of the disease. Long term illness usually leaves permanent physical residues, and most certainly produces memory traces of the illness which when disturbing are considered to be traumatic events. Mastery of chronic disease thus becomes an organismic task of physiological and psychological adaptation.[2] The physician can rehabilitate the patient by helping him to master traumatic memories, to find a new adjustment to a changed internal and external environment, and to accept his total or partial invalidism as part of a new reality.

STATISTICAL ASPECTS OF LONG-TERM ILLNESS

The magnitude of chronic disease is really appalling. Over twenty-five million people in the United States suffer from disabling or nondisabling chronic disease. Each year the chronic diseases cause nearly one million deaths, and one billion days of disability. Victims of these diseases occupy 750,000 hospital beds and receive the equivalent full-time services of at least one third of our physicians.[3] In the last war approximately one-third of all selective service registrants between the ages of 18 and 37 years were rejected for defects and diseases of primarily chronic nature.[4]

Furthermore, the age of patients, mortality, morbidity and duration of disability are steadily increasing. According to Halliday,[5] the rising incidence of psychosomatic affections is accompanied by a shift towards the younger age groups. Diseases which fifty years ago showed distinctly different frequencies in the two sexes tend to show a more equal distribution, which fact concedes with the progressive equalization of habits of males and females in our society. One half to two thirds of all the patients seen in practitioners' offices either have complaints of psychogenic nature or their symptoms are the result of noxious habits.

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and maladjustment Nearly 40 per cent of patients admitted to hospitals for chronic disease and old age suffer concomitantly from mental complications [1] Measured in any terms, long-term illness represents a staggering burden to individual and society It constitutes a major challenge to preventive and rehabilitative skills of medicine

THE CONCEPT OF HEALTH

The prime endeavor of physicians is to restore health The concept of health includes physical, psychological and social criteria From a physiological viewpoint health can be assessed by measuring the efficiency of the body or of organs for a given purpose (optimal function) [12] From a social standpoint one can describe as normal whatever coincides with the statistical measures of central tendency (comparison of individual function with group average) Psychologically speaking, however, we have to use standards which measure the flexibility and adaptability of an individual to a given situation These are as yet very tentative because the study of psychological and social functions has just begun However, one can say definitely that if a person is afflicted with a disease and continues to live, restoration to health depends upon whether or not bodily, psychological and social functions can be utilized for an integrated response If such is the case, further psychological and social growth is likely in spite of disease or invalidism and the person can be considered to be healthy If, however, one organ or system interferes with proper adjustment, the individual can be said to be sick An example might illustrate the case If somebody's health can be restored by means of an amputation, thus enabling this person to resume his duties in society, there is restoration to health, and medicine considers the therapy a success If, however, this same person continues to complain and does not resume his duties in society, the patient can be considered to be sick Therefore, adjustment of both body and mind to the changed internal and external environment seems to be a pertinent criterion of health This viewpoint is represented by Menninger,[11] who defines mental health as the adjustment of human beings to the world and to each other, with a maximum of effectiveness and happiness Not just efficiency, or just contentment—or the grace of obeying the rules of the game cheerfully It is all of these together, it is the ability to maintain an even temper, an alert intelligence, socially considerate behavior and a happy disposition In assessing the socio-psychological adjustment of a person, the following criteria[22] prove helpful.

Mental health is characterized by

(1) Freedom from physical, mental and character symptoms,

(2) Insight and awareness into motivations, needs and desires of self

as well as knowledge of limitations and awareness of impact upon others,

(3) Experimentation with reality through permanent testing and retesting of all possibilities and approaches,

(4) Gratification of wishes and self-expression,

(5) Conformance with and acceptance of the existing culture without paralyzing the spontaneity of expression and action,

(6) Tolerance for frustration in presence of adverse and traumatic situations,

(7) Ability to postpone immediate pleasures for the sake of long term goals,

(8) Mastery of the means of expression and communication,

(9) Integration and utilization of life experiences

SOCIAL AND CULTURAL ASPECTS OF LONG TERM ILLNESS

Acute disease is glamorized Ambulances rush with howling sirens through the streets, interns and attendants dressed in white take care of accidents, emergency wards are ready at any moment's notice, spectacular rescues and operations are publicized by radio and newspapers The dramatic aspects of acute disease capture the mind of the public and sacrifices of money and time are willingly undertaken by and for victims of emergencies

Long term illness, in contrast, has been treated for a long time as the stepchild of modern medicine In medical schools, teaching is still geared to acute conditions while chronic diseases are relegated to the back wards Patients with the garden variety of complaints such as headache, backache, fatigue, tension or pain are rarely presented in medical rounds, although they comprise the bulk of the cases in private practice The high-cost modern hospital is geared to take care of acute conditions Hence, administrators can rarely afford to keep a patient for a longer period of time and hospitals built to suit the needs and the pocketbooks of patients with long term illness are few in number If such exist at all they are usually reserved for patients suffering from infectious diseases such as tuberculosis or poliomyelitis, while persons afflicted with degenerative diseases are frequently neglected A clear-cut discrepancy exists between the effort put into the management of chronic disease and its statistical importance

Long term illness is a serious economic problem Rehabilitation frequently fails because patients can not be made independent from their source of support insurance companies relatives or charity organization In acute diseases everybody is willing to pay the necessary sacrifices because they are temporary well defined and rewarded by tangible results In long term illness in contrast results are rather not forthcoming

or are forthcoming much later, so that the premium paid is rarely related in the minds of people to the success obtained Only "better-to-do" people can afford long-term illness The uninsured person who relies upon earned income may become the victim of anxiety and feelings of insecurity which in turn impede successful rehabilitation

Closely related to economic problems is the attitude of people toward physicians These attitudes can be summarized best under the concept of social class structure [17 18 20] The way money is spent, the type of houses lived in, the property possessed, the family structure adhered to, the occupation which is followed, the associations which are cultivated, the education which is received, the ideology and interests which are followed, are highly correlated features In the lower class, for example, the patients keep away from physicians and medicine and apply for help in cases of emergency only In the middle class, overemphasis on health, cleanliness and body care prevails, thus leading to a crowding of physicians' offices In the lower class, disease is taken as a stroke of bad luck, while in the middle class anxiousness accompanies disease, and injury is taken as a personal affront to one's pride [21] In the lower class, the physician not only represents the healer and skilled technician, but he is also the representative of those who have, who know, and who can give Since freedom of expression prevails in the lower class, the physician does not substitute for interpersonal relations In the middle class, in contrast, where conformance may obliterate self-expression and where the ideal of smooth behavior may induce play-acting of mature behavior, the relationship to the physician frequently may constitute the only contact where the patient can let go and give up pretenses The physician then becomes the sole individual with whom personal problems can be discussed, thus rendering considerations of skill and medical knowledge less important [18 20]

National and cultural ideals also influence health [25] In the American society there is an emphasis on youth, beauty and action, and the majority of persons do not look forward with any degree of equanimity to old age In contrast, in China[3] old people are treated with respect and veneration, thus providing many more compensations for becoming old Consequently, in China fewer persons develop clear-cut psychoses of old age as compared to the United States Another American ideal is success in terms of acquisition of wealth or popularity Disease and disability rarely contribute towards success in these terms and patients then feel rather frustrated In contrast, there are European and Asiatic cultures where introspection and wisdom are highly respected values There the sick can attend to these aspects of life and gain some compensation for their disability

ADJUSTMENT TO DISEASE

The way a human being lives is in part responsible for the disease he is going to contract. This is clearly shown in occupational diseases and in illnesses which are related to the habits of man, such as eating, drinking, smoking, overexertion, or promiscuity. The personality thus determines habits which may be harmful to health. In a more subtle way these practices, through innumerable repetitions, seem to predispose the organism to certain diseases: certain systems or organs are used or abused more than others and may become exposed to noxious agents and degeneration.[4] Inasmuch as there is a definite relationship between personality and choice of disease,[23] it is not surprising to find that recovery from these diseases, in turn, is also related to personality factors.[1] If, for example, an aggressive individual who tends to overexpose himself to dangers[18] also disregards instructions of physicians and ignores precautionary measures in the recovery period from an accident, he might prolong convalescence considerably. In general, one can say that the more tense the person the less his adaptability to disease, and the longer the period of recovery will be.

The type of disease contracted influences the personality of the patient in different ways. A person whose major self-expression lies in the field of locomotion will be affected much harder by an amputation of the extremity than the passive, receptive personality. A person who overeats and suffers simultaneously from hypertension will be hit much harder by restriction of the diet than persons whose gratifications have never been in the direction of food intake. In general, one can state that disease frustrates an individual and that the frustration incurred acts as a motivation for finding new and compensatory ways of adjustment. Blindness, for example, requires a compensatory adjustment of auditory and tactile perception. Whenever patients are able to utilize frustration for adjustment, recovery tends to be uncomplicated. If, however, the frustration acts as a reward for self-destructive or dependent tendencies it reinforces invalidism.[17] Patients who have at their disposal the necessary adjustment patterns to master new situations and who do not suffer from any psychopathology can be rehabilitated with comparative ease. The essential process which takes place is one of learning new patterns and modifying old ones. There exist numerous rehabilitation centers, vocational guidance centers and vocational training schools, as well as agencies concerned with the selection and placement of handicapped people.[4] As such may be mentioned the schools in existence for the blind, the deaf, the amputee, the schools for spastic and crippled children, for victims of poliomyelitis, the facilities available for epileptics, and the schools and centers which were developed for the war injured.[4] Here medical skill

of specialists is combined with the psychological skills of people trained in rehabilitation

Chronic illness usually changes the interpersonal relations between people The blind, the deaf and the lame, for example, cannot communicate freely and cannot engage in unrestricted activities This handicap frustrates the need for group membership and patients tend to suffer from isolation and feelings of inferiority This factor can be appropriately taken care of only by placing people with similar handicaps and diseases into groups There they may share, partake, communicate and exchange For example, diabetics eat at special tables, the deaf communicate by means of sign language with other deaf people, while the blind learn to compensate by means of acoustic and tactile perception Enabling the sick to live or to congregate in groups which resemble as closely as possible customary social constellations is of prime importance If this is accomplished the patient will, in order to obtain group membership, learn the necessary steps and compensatory mechanisms from and with others Cues and tricks are taken over from those who have suffered from similar experiences, and planless experimentation—wasteful in energy and time—is supplanted by planned learning through imitation and copying

ANXIETY AS REACTION TO DISEASE

Since it is impossible to discuss all appropriate and inappropriate reactions to disease within the scope of this paper, the discussion shall be confined to the problem of anxiety only

In animals there exist warning signals which when perceived instigate psychological as well as physical preparedness for action This alarm reaction is designed to eliminate interference through fight or to avoid danger through flight The alarm reaction is a total organismic reaction designed for self-preservation In human beings the feelings engendered by an alarm signal are called either anger, fear or anxiety The differentiation of anxiety states from fear and anger is characterized by the ability to act In anger, impending danger or interference have been perceived as threats which can be managed, fought or conquered Action is contemplated or already undertaken and the behavior of the organism has been coordinated for this purpose In fear, integrated action is initiated to avoid the interference If coordination for fight or flight is impossible, fear or anger change into anxiety

A so-called anxiety state develops when the individual feels helpless or immobilized or when action becomes impossible either because of self-inhibition or because of overwhelming environmental press Then the massive impact of stimuli upon the organism, the feeling of danger and the expectation of defeat become so overwhelming that the individual

feels paralyzed. As a result the preparedness for action cannot be consummated and vascular, muscular, respiratory and endocrine phenomena persist for undue lengths of time. This condition is felt by the organism as anxiety and tension.

Since disease affects the internal environment, flight or fight are impossible. After all the necessary and possible steps to restore health have been undertaken and the individual is still threatened by disease, it is understandable that anxiety may be the result. Noncurable or chronic sickness may last for many years before leading to ultimate death, but the certainty of this event is permanently kept in front of the patient. Although he may outlive his healthy contemporaries he still feels threatened twenty-four hours a day. It is part of the task of rehabilitation to make the patient tolerate the dangers inherent in his disease, just as the ordinary human being is able to master the threats confronting him in a modern technical civilization.

The psychological management of anxiety is the most essential therapeutic step in any disease. Not only happiness and joy of living depend upon freedom from anxiety, but the physical concomitants of anxiety have untoward effects upon physiological processes in the body. Hence it is not surprising to see that surgeons[13] make use of this knowledge by preparing their patients before operation in a way which will reduce anxiety to a minimum. Every physician attending to chronic diseases has to depend upon management of anxiety for achieving results with his patients.

Manifestations of Anxiety.—A short summary of the manifestations of anxiety will illustrate the possible damage which anxiety can do to the already diseased body, thus interfering in a devastating manner with the healing process.

Predominantly vascular. Increased blood flow in brain, heart, lungs, muscles. Decreased blood flow in abdomen, contraction of spleen. Increase in heart rate, arrhythmias, palpitation in the heart region, increased blood pressure. Headache, knocking, pressing or fullness in head. Increase of red blood cells in circulation. Acceleration of coagulation of blood.

Predominantly bronchial or endocrine. Adrenalin output into circulation, insulin tolerance increased. Disturbance of female cycle.

Predominantly respiratory. Increase in metabolism expressed in increase in respiratory volume and oxygen consumption, shallow rapid breathing, air hunger, sighing, yawning. Respiratory alkalosis, vertigo, giddiness, faintness. Dilatation of bronchioles, spasmodic coughing.

Predominantly muscular. Increased muscular tension expressed in exaggerated tendon reflexes, tightness in throat, neck and chest, jellied knees, tremor, trembling, general restlessness and desire to move, strained or worried expression. Subsequently tension can change into weakness and inability to move. An anxiety state can be conceived as

the tense expectation of the startle reflex it consists of the involuntary, unconscious flexor spasm involving face, trunk and axial apendicular musculature, it is unchanged by habituation and lasts less than one second [10]

Predominantly secretory Gastric hyperacidity, increased salivation, sweating, tearing and crying, white flow

Predominantly gastrointestinal Hyper- or hypomotility expressed in spasms, constipation or diarrhea Gastric and intestinal hypersecretion, nausea, heartburn, hunger, swallowing of air

Predominantly genitourinary Urinary urgency and frequency, white flow, itching in urethra, impotence, frigidity

Predominantly skin Blushing, blanching, blotching, pilomotor erection, sweating, parasthesias, sensation of warmth or cold

Predominantly sensory General clouding of alertness and dulling of level of consciousness, diminished response to osmic, visual, auditory, gustatory, tactile, temperature, pain and vibratory stimuli, except for that sensory area where stimulation is expected and anticipated

Predominantly psychological Insomnia or sleepiness, feeling like dying, like being mutilated, anticipation of impending disaster Expectation and anticipation prevail over reminiscence

Extreme anxiety or panic Paralysis, fatigue, fall in blood pressure, fall in heart rate, peripheral dilatation following constriction, vasodilatation of abdominal region, incontinence of urine and feces, and, ultimately, shock or death follow the features discussed above

THE MANAGEMENT OF ANXIETY

The application of long-term psychotherapeutic procedures falls into the field of psychiatric care However, the management of anxiety arising in connection with disease is the function of the attending physician The ability to alleviate anxiety is a property common to all healthy persons An example from daily life may illustrate this point A child when frightened by an apparently dangerous event, such as a big dog charging or a bird fluttering close by, runs to the mother If she is a mature person and free of anxiety she will pick up the child or hold it by the hand or talk gently and almost instantaneously this action will alleviate the tension However, if the mother herself is anxious, she will not be able to alleviate the tension, on the contrary, she tends to aggravate the anxiety of the child Basically, interpersonal relations are entered into because contact with other persons alleviates anxiety and tension, and thus in the course of maturation of the child the ability to alleviate anxiety by a non-anxious adult forms the basis of all later interpersonal relations It is quite obvious, then, that a patient who has, on the whole, good interpersonal relations but is stricken with a chronic disease will use the mechanisms of communication and of personal contact to alleviate anxiety regarding problems such as death, disability, invalidism and insupport

The patient, however, can only communicate and express his tension if the attending physician is free from anxiety If, however, the doctor is an anxious person he will be unable to relieve the patient of his tension In watching eminent physicians at work it becomes obvious that their success is frequently due not so much to their technical skill as to their ability to establish good interpersonal relations, thus alleviating tension of patients in critical situations As a result, the relatively relaxed individual will tolerate most therapeutic procedures without complications Considering all the pathophysiological concomitants of anxiety it becomes quite obvious that physicians "who have the full confidence of their patients" have at their disposal most potent means of influencing in a beneficial way most organs and organ systems of the human body

Freedom from anxiety is based on several factors The history of people who are relatively nonanxious usually reveals a mother or father who was able to alleviate anxiety either by means of verbal or nonverbal communication Associated with this feature there existed in these families a certain freedom of expression Father and mother were able to admit that at times they felt angry, fearful or anxious and they did not attempt to project, rationalize or hide this fact from the child Emotions thus were admitted to the family life as an essential part of living, and control did not enter at the level of perception and expression of emotions but on the level of subsequent action The youngster learned at an early age that anger is a warning signal requiring appropriate action and that pleasure means that particular behavior is becoming to the individual In these families emotional maturity was attained because pleasure, displeasure, anger, anxiety, fear shame, guilt and depression were utilized for initiation of appropriate behavior

In contrast, in those families where this freedom of expression did not exist the children never learned to utilize their emotions as indicators of behavior Psychologically speaking, they remained immature[24] being unable to integrate emotions with subsequent actions Since expression was punished the child soon felt that emotions were a nuisance rather than a useful biological mechanism for adjustment In such families anxiety of the baby was not alleviated and crying of the child was not considered a communication but a necessary evil Such parents adhered to such popular misconceptions as that alleviation of anxiety constitutes indulgence They did not know that if mother is ready and available when the child cries the youngster will learn to manage anxiety in interpersonal relations However if the anxious child is left to himself he must develop internal control mechanisms to overcome this anxiety These initial defense mechanisms will later prevent an individual from establishing good personal relations because restraint and control will always be of greater concern than self-expression communication and

understanding of self and others Such individuals perform poorly under stress and strain, since anxiety is likely to break through because control mechanisms usually lack diversification This rigidity contrasts with the flexible behavior of people who learn to communicate and to handle their anxiety in interpersonal relationships Such individuals have the ability to drain anxiety little by little, and catastrophic events with tremendous increase in tension can thus be managed without breakdown

Anxiety is one of the most infectious conditions If one person is anxious it is immediately transmitted consciously or unconsciously to others The best example of the infectiousness of anxiety is found in panics occurring at times of civilian catastrophies, accidents and wars Similar, but less obvious, is the transmission and communication of controlled anxiety The reaction on the part of the recipient is more akin to anger and annoyance than to fear and anxiety These outwardly calm people in their rigid need for control transmit to others the effort involved in maintaining relaxation The other person then reacts to the effort involved, since it is understood that the situation is potentially so dangerous that it marshals all the resources of an individual for the sake of control The response, of course, is anger or anxiety

In the presence of long-term illness freedom from anxiety on the part of both patient and physician constitutes the ideal basis for any rehabilitation The necessary adjustment dictated by invalidism and limitation of function can be undertaken, because the efforts of the individual will be concentrated upon learning and relearning rather than upon the management of anxiety A good doctor-patient relationship thus makes implementation of therapy easy Different is the situation when one of the two participants transmits anxiety to the other If the patient is faced with a slightly anxious, overprotective, restrictive or punitive physician, insecurity will be engendered The reverse occurs when the insecure patient inoculates the physician with anxiety, while the worst situation is met when severe psychopathology on the part of the patient or physician is encountered In such cases the principal problems met with are those of cruelty and suffering A patient whose past experience favored the establishment of interpersonal relations by means of self-abasement and subordination is stimulated by disease or accident to continue these masochistic and self-destructive tendencies [19] Such a patient will be relatively anxiety-free as long as he suffers, but as soon as things go well he tends to become increasingly anxious until the condition grows worse again Thus, disease and ill health in some way gratify and ease his anxiety, while the therapeutic effort of the physician, when successful, becomes frustrating to the patient In turn, the therapeutic ambition of the physician is challenged and usually he does not know what he is up to The patient seduces the physician into becoming cruel, in terms of punitive behavior, unnecessary restrictions or unnecessary surgical or

medical procedures The doctor patient relationship then is characterized by the introduction of neurotic needs on the part of both participants the doctor demonstrates his need for cruelty, dominance, glory, approval or prestige or, conversely, the need for feeling wanted, needed, abused and indispensable The patient in turn demands more and more diagnostic and therapeutic measures and the symptoms of the neurosis of both patient and doctor become somehow complementary In this mutual adaptation both persons feel comfortable, but it is the end of rational medicine and a great deal of harm can be done Psychiatric treatment, at least for the patient if not for the physician, is indicated in such cases This example illustrates fully the importance of personality assessment and character training in the selection and education of the medical student Freedom from anxiety on the part of the physician has to be achieved if the fullest potentialities of a medical man are to be developed

SUMMARY

Long term illness constitutes a field of medicine which is concerned with chronic diseases, recurrent diseases invalidism following trauma or illness and infirmities of the aged In the United States one person out of six suffers from such conditions Hence, it represents a most important but up to now neglected field of medicine

In contrast to people afflicted with acute diseases, bearers of long term illnesses as an additional burden have to modify for purposes of survival their social techniques habits attitudes and beliefs This process of social learning can be facilitated by hospitals and physicians in various ways First, provision must be made for the availability of technical skill for rehabilitation of the body Second a good doctor patient relationship represents one of the principal tools to induce the patient to use his invalid body the best he can Third, whenever possible a setting should be provided in which the prevailing values that ordinarily govern life under healthy conditions have already been modified in such a way as to suit the needs of the sick person Implicitly, then, will the patient be imbued with this new viewpoint which will be beneficial to his condition Fourth there should be an opportunity for the patient to become a socialized member of a group in which the other participants also suffer from similar handicaps He then will be among equals and his need for group membership will speed up the processes of rehabilitation The combination of these four factors then will provide the necessary grounds so that a patient can proceed to master in a socialized manner the difficulties inflicted by his handicap

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HEPATIC INSUFFICIENCY

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INTRODUCTION

The subject of subacute and chronic liver disease is still confused and obscure as far as the clinician is concerned. We are still in that stage of knowledge where only the advanced and terminal forms are readily and frequently recognized. Cirrhosis of the liver with ascites and massive hemorrhage presents a well known clinical picture but the less severe forms of chronic liver disease are usually not diagnosed. Yet it is probable that various types of low grade chronic liver disease are quite common. We know that liver injury may be produced by a great variety of infections, toxic conditions, metabolic disorders and hepatotoxic drugs and chemicals and it is only reasonable to expect that chronic disease and permanent damage not infrequently occur. Our failure to recognize these cases clinically is apparently due to an absence of a clearly defined and well established clinical picture. Symptoms and physical findings are not striking and definitive laboratory procedures are often lacking. However, it does not seem reasonable to us to assume that disease of an organ which plays such a varied and important role in the body economy as the liver is entirely "silent" and without clinical manifestations.

It is interesting and instructive to recall that the liver used to be held responsible for many complaints, as the old terms of biliousness, liverishness, and sluggish or torpid liver bear witness. However, with the advent of modern scientific medicine at the turn of the century these diagnoses lost favor apparently because they could not readily be verified. Only an occasional astute clinician such as Hurst[1] or Bloomfield[2] continued to point out their clinical importance.

During the last ten years considerable light has been thrown on this obscure field. It is now possible in many instances to recognize clinically, cases of early chronic liver disease. This is of obvious importance. From the therapeutic point of view. We cannot hope to alter irreversible pathologic lesions but it is possible that the development and progression of cirrhosis can be delayed or arrested. Secondly, liver trauma incident to surgery or due to exposure to hepatotoxic chemicals or drugs may be modified or avoided. In the presence of preexisting liver damage either

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symptomatic or latent, such trauma may have serious or even fatal results Finally, the cause of otherwise obscure symptoms may be clarified and more rational treatment adopted

Our knowledge of this field has been advanced principally because of the recent interest in viral hepatitis and of the opportunities for study provided by the large number of cases of this disease that have occurred since the beginning of World War II Chronic viral hepatitis has become a definite clinical entity although it is still far from being completely understood Fortunately, the clinical response of the liver to different injurious agents is often quite similar so that considerable light has been thrown on chronic hepatitis of other etiology Because we believe that this important field of early chronic liver disease has received inadequate attention especially among clinicians we propose to limit this paper to a discussion of this subject

CHRONIC VIRAL HEPATITIS

Only recently has the existence of a chronic form of viral hepatitis received general acceptance For some years occasional cases have been reported in the literature,[3] [4] and evidence has been presented that persistent liver dysfunction may follow acute viral hepatitis [5] [6] In 1938 Bloomfield clearly postulated the existence of such a condition by a careful analysis of the case histories of cirrhotics [2] It was not until 1945, however, that a careful clinical study based on adequate material was published [7] Subsequently a number of other excellent papers have appeared [8] [9] [10] [11]

Definitions and Pathogenesis —We have arbitrarily applied the term "chronic" to any case with persistent evidence of liver disease lasting more than three months from the onset of the acute attack Although the pathogenesis is not definitely established, Neefe[12] has recently found that the virus may remain in the liver in chronic cases for from three to twelve months This confirms our clinical expectations As a rule, chronic hepatitis develops in patients who have received poor treatment, in persons with previous liver damage or in those with secondary infections, undernutrition or some other complication In many instances no explanation is apparent and perhaps it is due to inadequate immunity or to some characteristic of the virus

The histopathologic picture has been carefully described by a number of authors [8] [13] [14] [15] Round cell infiltration in the periportal areas is perhaps the most common finding, although the inflammatory reaction is often more extensive Increased connective tissue may develop The so-called cholangiolitic form presents a special picture [16] Finally, there are definite clinical cases with normal biopsies [15]

Clinical Picture and Course —This we have previously described in

detail? Briefly, chronic hepatitis may follow directly after an acute attack or may appear as a relapse after apparent recovery. It is to be emphasized that the acute attack is often mild and without jaundice. We have repeatedly observed cases of this sort[17] and in some instances the diagnosis has been confirmed by liver biopsy.[18, 19] The danger of chronicity following acute hepatitis without jaundice is undoubtedly enhanced by improper treatment resulting from a lack of recognition.

The course is usually characterized by exacerbations and remissions, although this is not necessarily the case. There is always a tendency to chronicity, as shown by the slow response to therapy as compared with acute cases. Clinical recovery may occur after two to three months or the disease may continue indefinitely. Clinical jaundice is usually absent except in the cholangiolitic form where it is often intense.

Active and Inactive Hepatitis.—One of the most striking clinical facts regarding this disease and one that has caused much confusion is the apparent discrepancy between the laboratory evidence of liver injury and the severity of symptoms. Although we still do not understand the basic physiologic reasons for this phenomena, there is considerable evidence pointing towards a practical clinical explanation.

We originally pointed out that the severity of symptoms was directly related to the degree of liver tenderness[17] and have referred to this as 'activity' of the hepatitis. Thus, cases have been separated into those of active hepatitis with symptoms and liver tenderness and those of inactive hepatitis with minimal or no symptoms and no liver tenderness. Naturally in the latter group there must always be objective evidence of liver disease else the term hepatitis is not applicable.

This distinction is best demonstrated by the characteristic response to physical exertion of the patient with active hepatitis.[17, 18] Exercise especially of a jolting nature is followed by an increase in liver tenderness and often liver size by an aggravation of symptoms and by laboratory evidence of increased liver dysfunction which typically persists for at least several days. In essence this response constitutes a relapse of the disease and it may continue to progress for a week or more even though the patient is put to bed. As would be expected, the corollary is also true, namely that symptoms and abnormal physical and laboratory findings improve or disappear with bed rest. In the inactive case no significant response can be obtained to either exercise or bed rest.

Since a self perpetuating clinical relapse can be produced, it is most reasonable to assume that an active infection is still present in the liver as suggested by the Fisher and Neefe.[5] Furthermore, the clinical picture seems to fit the concept of an inflammatory process in the liver. Popper and his associates have recently [illegible] that [illegible] liver [illegible] actively [illegible] an inflammatory [illegible]

Thus it would appear that activity is related to a type of inflammation that produces symptoms and that is probably associated with a continuing infection with the virus, while inactive hepatitis is a more static condition and possibly represents residual and often permanent damage Both lesions can account for alterations in liver function tests although the pattern is somewhat different

The determination of the degree of activity and the response to exercise have a great deal of clinical value Thus, exercise may make latent findings manifest and so make a diagnosis possible Likewise, the therapeutic benefit to be expected from bed rest can be judged from the degree of activity or the response to exercise Finally, this concept aids in the evaluation of recovery Thus activity of the hepatitis may be masked by bed rest only to recur when the patient is again allowed to be ambulatory Rest must be sufficiently prolonged to prevent this happening True recovery is, of course, associated with a negative response to exercise

TABLE 1

SYMPTOMS ASSOCIATED WITH CHRONIC ACTIVE HEPATITIS

1 Lassitude and fatigue
2 Gastrointestinal symptoms
    Anorexia
    Fat intolerance
    Flatus and belching
    Intestinal cramps—spastic bowel
    Loose stools
3 Liver ache or pain
    Right upper quadrant ache or heaviness
    Right lumbar ache
    Poorly localized pain in right chest
4 Vasomotor symptoms
    Dizziness
    Easy sweating with emotion or exercise
    Hot flashes
    Generalized pruritus, "goose pimples" or miliary urticaria with heat or excitement
    Oral hyperthermia
5 Mental symptoms
    Depression and confusion
6 Headache
7 Probable endocrine symptoms
    Menorrhagia
    Impotence

Symptoms —In Table 1 we have listed those symptoms which we believe are specifically a result of the disease This has been determined by making observations during periods of changing activity, especially the acute changes artificially induced by exercise followed by bed rest The

presence and severity of these symptoms have repeatedly been found to correlate with the degree of liver tenderness and with the results of laboratory procedures.

Lassitude is easily the most common and the most disabling complaint associated with active hepatitis. It is not ordinary easy fatigability but rather a kind of inertia. Even after a good night's rest the patient has no ambition. It is almost always present in some degree. Aching in the region of the liver or in the right lumbar region is also characteristic but there should be a definite history of aggravation from exercise or jolting activity with persistence for several days.

The symptoms associated with inactive hepatitis are fat intolerance, belching, and indigestion. When marked weight loss is present there may be weakness and easy fatigue. Rarely is there significant disability and

TABLE 2

ABNORMAL PHYSICAL FINDINGS WHICH MAY BE PRESENT IN CHRONIC HEPATITIS

A. Mild and moderately severe cases
1. Hepatomegaly
2. Liver tenderness to palpation and percussion
3. Tenderness in right costovertebral angle
4. Splenomegaly
5. Jaundice
6. Spider angiomas
7. Liver palms
8. Adenopathy

B. Additional findings in severe cases
1. Gynecomastia and testicular atrophy
2. Ascites
3. Peripheral edema
4. Dilated collateral venous channels
5. Purpura
6. Fetor hepaticus

often there are no complaints at all. Naturally, there are cases with only mild activity that fall between the two extremes and these may present atypical pictures.

Physical Findings. In Table 2 are listed the abnormal physical findings which may be present. Liver tenderness, best elicited by direct fist percussion, is almost always present in active hepatitis unless the patient has been in bed long enough to allow subsidence of activity. Often liver ache or pain is observed to develop slowly and to build up for some ten to fifteen seconds after the percussion and then to persist for at least several minutes or even several hours. This type of reaction is in our experience almost pathognomonic of true liver pain.

Laboratory Findings. Owing to the multiplicity of physiological functions possible in the liver, methods of measuring liver function

are myriad In chronic hepatitis it is desirable to employ a group of tests, since a variety of patterns can be observed and single tests are not reliable, particularly when negative For the average clinician it is best to select four or five procedures rather than a large group and to employ them repeatedly both in the same and different cases Normal standards for the particular laboratory then become apparent and the evaluation of abnormal results is improved For obvious reasons we can only present here a summary of those methods which in our experience have proved to be the most valuable

In Table 3 is listed a group of tests with technical references which have been divided into "preferred" and "optional " Those in the first group can be performed in any reasonably well equipped laboratory, are

TABLE 3

LABORATORY TESTS IN CHRONIC VIRAL HEPATITIS

Test	*Method*
A Preferred	
1 Bilirubinuria	Methylene blue[7, 21]
	Strip test[22]
2 Bilirubinemia	Modified van den Bergh[23]
3 Urobilinogenuria	Watson's 2 hr quantitative[24]
4 Bromsulfalein	5 mg /kg [7]
5 Thymol turbidity	Maclagan[25]
6 Serum albumin and globulin	Any standard method
B Optional	
1 Serum alkaline phosphatase	Bodansky[26]
2 Cephalin cholesterol flocculation	Hanger[27]
3 Gold sol	Gray[28]
4 Urine coproporphyrin	Watson[29]
5 Hippuric acid synthesis	(See Ref 30)
6 Cholesterol esters	(See Ref 31)

reasonably reliable and at the same time fairly sensitive and specific for the liver There are various objections to those in the second group including technical difficulties, especially in the case of No 4 and 6 and unreliability in No 5 [19] The alkaline phosphatase determination should perhaps be included in the preferred group, but it is not specific for liver disease

Bilirubinuria and an elevation of the prompt direct reacting serum bilirubin are often associated and are indicative of a moderately severe degree of clinical activity and the presence of inflammatory changes They are extremely significant findings, diagnostic of liver injury provided that extrahepatic obstruction can be ruled out Elevation of the indirect reacting serum bilirubin is much more common and can occur in both active and inactive forms In our experience it almost always

indicates liver injury, although not necessarily severe, *provided that* increased blood destruction is ruled out

Quantitative estimation of the urine urobilinogen is a most sensitive and specific test of liver function Watson's quick method [illegible] is easily performed in the office It is best used in a serial manner It may be elevated in both active and inactive hepatitis

The bromsulfalein test is in certain respects our most quantitative test Readings should be made at both forty-five and sixty minutes as a check In our experience, values of 3 per cent or more in sixty minutes or 4 per cent or more in forty five minutes may be considered as abnormal,[7] especially if both figures are in this range This test, however, does not give information concerning the nature of the liver lesion or the degree of activity

The thymol turbidity as well as the alkaline phosphatase test is usually associated with clinical activity Separation of the serum proteins is valuable because an elevated globulin is frequently found in active hepatitis. But more important, a significant lowering of the serum albumin level is strongly suggestive of relatively advanced cirrhosis

For a detailed discussion of biopsy findings the reader is referred to previously mentioned papers

Diagnosis —The requirements for a diagnosis of chronic active viral hepatitis are (1) objective evidence of liver disease (2) symptoms consistent with the diagnosis and (3) a past history of acute hepatitis [illegible] It is difficult to define strictly each of these items In some cases one is justified in accepting a large tender liver as evidence of liver disease, but usually it is best to have laboratory or histologic evidence as well Liver tenderness must be present of course unless the patient has been in bed or on a limited amount of exercise Unless a history of acute icteric hepatitis is obtained the diagnosis is questionable except when the acute nonicteric attack was personally observed by a competent physician A diagnosis of acute nonicteric hepatitis cannot be definitely made from a history alone although it can often be strongly suspected An illness of three or four weeks or more with typical symptoms aggravated by exercise is particularly suspect [illegible] It is also necessary that the chronic illness follow the acute attack within a reasonable time If symptoms even though mild are present during this interval it may be as long as a year but if apparently complete symptomatic recovery follows the acute attack then the present illness should follow within a couple of months

Inactive hepatitis differs only in the relative absence of symptoms in the absence of liver tenderness and in not being affected by exercise [illegible]

The relative [illegible] to be [illegible] the different diagnostic points depends [illegible] In the case when the history is clear cut symptoms are

typical and liver tenderness is present, we are willing to make the diagnosis even though the laboratory findings are equivocal and the biopsy negative On the other hand, when any of the former are equivocal, then laboratory evidence is essential It cannot be too strongly emphasized that the clinical picture, the course of the disease and the reaction to varying degrees of exercise are relatively uniform and constitute an easily recognized clinical syndrome, although perhaps not a striking one

Differential Diagnosis.—Chronic viral hepatitis is often confused with *chronic cholecystitis* and a group of *functional gastrointestinal disorders* [33] In the first instance this is because of a history of fat intolerance associated with a dim or absent gallbladder shadow by the Graham-Cole test [33] This latter finding, which is due to the inability of a diseased liver to excrete the dye, needs emphasis In our experience the liver damage must be moderately severe and the bromsulfalein retention is usually 10 per cent or more in one hour after 5 mg/kg However, there is not a constant correlation

The findings of gastritis, duodenitis by x-ray,[33, 34] an irritable and spastic gut, the presence of increased flatus and loose stools in hepatitis lead to confusion with a variety of gastrointestinal conditions Errors in diagnosis can be avoided only by always considering the possibility of hepatitis and, if the picture warrants, performing the appropriate tests It is not improbable that many obscure gastrointestinal conditions are actually on an hepatic basis

Psychoneurosis is the other important differential diagnosis This is largely due to the symptom of fatigue, the depression and mental confusion and the evidence of vasomotor instability The situation is further confused by the frequent presence of psychoneurotic factors as in all chronic diseases Nevertheless, we believe that it is usually possible to distinguish between the psychoneurotic symptoms and those due to liver disease The differentiation rests primarily on an evaluation of the degree of activity of the hepatitis since clinically this determines the severity of these particular symptoms To establish hepatitis as the cause of these symptoms it is not only necessary to have objective evidence of liver disease but also true liver tenderness If the hepatitis is inactive these symptoms are on a functional basis The response to exercise and rest may be of crucial importance Not only does it clarify the degree of activity but psychoneurotic symptoms are found to be affected in an opposite fashion to those of hepatitis For example, we have observed "psychoneurotic" liver tenderness disappear with exercise and "psychoneurotic" fatigue persist indefinitely or increase with bed rest

The final group of conditions that must be differentiated are the *other etiologic types of hepatitis* Etiologic agents include other infections,

chemical toxins, malnutrition, metabolic states and neoplasms. Often several etiologic factors are present simultaneously. This is especially true of chronic viral hepatitis because the presence of another hepatotoxic factor is frequently the cause of the chronicity of the viral hepatitis. Although the history of acute viral hepatitis leading directly to the present illness is presumptive diagnostic evidence, an absolute etiologic diagnosis is at present impossible because of a lack of specific tests.

Treatment.—Our treatment of chronic viral hepatitis is based on three cardinal principles, namely rest, diet and the eradication and avoidance of other liver trauma.[23] When such a regimen is carefully followed, satisfactory results are obtained in about 75 per cent of cases. Of this group some recover symptomatically and their liver function tests return to normal, but the majority go into an inactive or latent phase. These latter retain laboratory evidence of liver dysfunction but symptoms are minimal or absent and there is little or no disability.

Rest.—There can be little doubt concerning the value of bed rest in acute hepatitis, as we were the first to demonstrate.[19] Although results were not so striking, we obtained similar results in chronic active cases,[7] especially during the first year of the disease. Subsequent experience has confirmed these observations. Nevertheless, the value of bed rest is still not generally appreciated. In our opinion it is the most effective available therapy in the majority of active cases.

The benefit to be expected from bed rest in a specific case can be approximately determined by observing the response to exercise. Patients with active hepatitis are helped but those not affected by exercise and without liver tenderness, who have inactive hepatitis, receive relatively little benefit. In fact, it is not certain that rest has any therapeutic effect in such cases. Thus complete bed rest is necessary only in definitely active cases and no exercise restrictions are needed in inactive cases. In borderline cases partial restrictions are enforced depending upon the severity of the damage. Where liver damage is severe or where moderate restriction of activity is ineffective, complete bed rest should be tried.

Experience has shown that this treatment must be prolonged if a permanent remission is to be obtained. Thus a minimum period of two months is necessary, or a month after the disappearance of symptoms and liver tenderness and if possible the subsidence of abnormal laboratory findings. We have some evidence that even in cases of cirrhosis prolonged periods of bed rest are beneficial and may arrest the progress of the disease. It is noteworthy that many of Patek's[20] patients who were cured, with few, if any, were actually kept at bed rest. A limited exercise [illegible] percent, although this factor was not considered as having had [illegible] influence on the outcome.

Diet.—There [illegible] of the diet in chronic viral hepatitis is not clear

If adequate nutrition is maintained, it is doubtful whether the fat content[37] or even the protein content is of great importance For the present it is best, however, to maintain a protein intake of 125 to 150 gm a day, with carbohydrates of 250 to 300 gm and some restriction in fats, especially those derived from meat Eighty to 100 gm of fat, especially butter fat, is probably not harmful and is necessary for a palatable diet Often patients refuse to eat meat fats because of the resulting indigestion Fluid intake should be maintained between 2500 and 3000 cc daily If such a diet is taken there would seem to be no advantage in adding methionine or other similar substances We do not believe that any of these substances have been shown to be effective in well nourished patients with this condition

Elimination of Other Foci of Infection —The final therapeutic principle is perhaps the one most often overlooked The presence of other infections or foci of infection is frequently the cause for persistence of the hepatitis Abscessed teeth, badly infected tonsils, furunculosis, sometimes chronic pulmonary infections and severe dermatitis have all been actually observed to act in this manner Chronic malaria must always be suspected in persons who have been exposed A therapeutic test with quinine is advisable in case of doubt Amebiasis is perhaps the most common and the most important infection to be sought The incidence of amebiasis in cases of chronic viral hepatitis is considerably higher than in the population at large, probably because viral hepatitis is likely to become chronic if amebae are present We believe that, even though no amebae are found, a therapeutic test with emetine (1 grain daily for six days) should be tried, especially if severe symptoms or severe liver damage are present If there is a therapeutic response beginning on the third or fourth day, the drug should be continued for a total dose of 10 grains This is illustrated in the following case report and in Figure 149

CASE OF J L P —A 19 year old, white, male soldier entered the hospital August 31, 1945 complaining of marked fatigue and lassitude, mild anorexia and excessive flatus On about April 1, 1945 he began to have four or five stools each day punctuated by bouts of severe watery diarrhea Abdominal cramps were marked and no blood was noted in the stools On June 18 during a bout of diarrhea he developed nausea, vomiting and fatigue Although the severe diarrhea subsided in a few days, anorexia and lassitude persisted He noted jaundice first on July 5 and was hospitalized on July 10 The maximum icterus index was recorded as 104 on July 21 He was kept at partial bed rest The jaundice gradually subsided but the present complaints persisted

On admission the liver was palpable 5 cm below the costal margin It was markedly tender to palpation and percussion and there was tenderness in the right costovertebral angle As shown in Figure 149, both the prompt direct (one minute van den Bergh) and the total bilirubin were slightly increased while the

cephalin cholesterol flocculation, the bromsulfalein and the urine urobilinogen were markedly abnormal

Endamoeba histolytica was found in the stools and a course of 6 grains of emetine commenced on September 21 (seventy-eighth day) Liver tenderness, costovertebral tenderness and symptoms were markedly improved although the liver edge continued to be felt 3 to 4 cm below the ribs Laboratory findings became normal except for a 1 plus cephalin cholesterol flocculation in twenty four hours

On October 24 (111th day), after two weeks without symptoms and only borderline liver tenderness, the patient was allowed out of bed On November 14 (132nd day) he started the exercise tolerance test One week later following a strenuous week end at home without liquor he had a recurrence of anorexia, liver

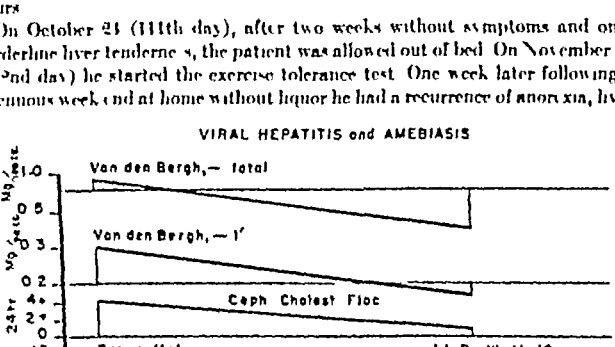

Fig 110 Progress of patient with viral hepatitis and amebiasis to emetine

ache and has tender associated with liver tenderness He was returned to bed because of the evidence of a beginning relapse

This patient apparently first had amebiasis and then developed viral hepatitis The relapse in the fifth month after exercise is strong evidence of persistent viral hepatitis although it is of course possible that the attack of fever was still present Although it is admittedly impossible to prove it is our strong clinical impression that in cases such as this the hepatitis is due to both the virus and the amebiasis Only after the latter is cleared up will the virus infection be manifest

If a patient is found to fail to respond to anti amebic therapy it

must be treated with all other available methods such as diet, bismuth or kaolin It can be stated as a rule that chronic hepatitis never recovers in the presence of chronic diarrhea Apparently diarrhea per se has a deleterious effect on the liver In fact we have produced a mild relapse with daily salts Since nontropical sprue is often a factor in long-standing chronic diarrhea, folic acid by mouth or crude liver extract intramuscularly is frequently effective In our experience it is in such cases that the intravenous liver extract of Hoagland and his associates[38] has produced results We do not believe, however, that it is usually necessary to administer the liver by vein

Toxic substances such as alcohol and arsenicals, exposure to hepatotoxic chemicals, and surgical procedures are to be avoided It should be mentioned that, regardless of what the exact role of alcohol in the etiology of cirrhosis turns out to be, there can be no doubt concerning its effect on chronic active viral hepatitis We have repeatedly observed that it produces a relapse

Other therapeutic measures as transfusions or the administration of serum albumin or plasma are necessary only in the more severe forms of the disease

OTHER FORMS OF CHRONIC HEPATITIS

Although extensive clinical data is not available regarding other etiologic forms of chronic hepatitis, there is good evidence that a true hepatitis occurs with many infections In some of these we have had opportunity to observe a clinical picture closely similar if not identical to that of chronic viral hepatitis In such instances it is only reasonable to assume that the symptoms are due to liver injury and that the treatment should be directed towards the liver

Amebiasis —In amebiasis we frequently can obtain evidence of liver dysfunction without the findings of abscess in association with the symptoms and physical findings of hepatitis This has been described by Klatskin[39] and by Shute [40] Following the administration of emetine the findings promptly disappear and the liver function tests improve as in Figure one

Malaria.—Here again there is ample evidence of liver injury [41] Although it has not been emphasized, the clinical picture in chronic malaria is often that of a chronic hepatitis Antimalarial therapy is, of course, indicated

Infectious Mononucleosis.—Although it is well known that this disease is almost always accompanied by acute liver injury,[42] [43] it is not generally appreciated that persistent hepatitis may develop In most cases of infectious mononucleosis in which convalescence is prolonged we believe that hepatitis is the source of the symptoms The clinical picture

is almost identical to that of virus hepatitis If acute infectious mononucleosis is treated as one would treat hepatitis, chronicity can usually be avoided and complete recovery accelerated A similar situation exists in connection with virus pneumonia[7, 19]

Brucellosis—Lesions of the liver including increased fibrosis have been demonstrated by Hoffbauer and Spink[44] in this condition Clinically, the picture of chronic brucellosis is often that of a chronic hepatitis There may be an exacerbation with exercise It is not unlikely that many of the symptoms in this condition are due to pathologic changes in the liver

Toxic Hepatitis—Wilensky[45] has described the syndrome of chronic hepatitis in industrial workers exposed to various hepatotoxic fumes In addition, it is common knowledge that many alcoholics manifest a similar picture

SUMMARY

The purpose of this paper has been to present the syndrome of chronic hepatitis as a reasonably clear-cut, recognizable clinical picture Although chronic viral hepatitis has been used as an example, there is reason to believe that many other etiologic forms present a similar picture Diagnosis of early chronic liver disease serves to clarify the cause of otherwise obscure symptomatology and offers the additional advantage that therapy at this stage is more likely to be effective The principles governing therapy have been discussed

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UROGENITAL DISORDERS OF THE AGED

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GENERAL CONSIDERATIONS

For the present study we are reporting our surgical experiences with 128 patients, 70 years of age and over, suffering various diseases of the genitourinary system. All of them were operated upon, involving 226 major surgical procedures, at the Morrisania City Hospital, New York, during the last two and one-half years. The age groups are shown in Table I. Only five patients were female. All demonstrated not only the senescent changes (normal or advanced) for their age group, but also dependent or superimposed diseases of the genitourinary tract.

It must be recognized that the physiology of the senescent is peculiar and, generally speaking, biologically retarded. In them the *power of* resistance is lowered and, consequently, inroads of pathological processes are enhanced. It is necessary to differentiate clearly between intercurrent disease and senile changes which cannot be altered. It has been shown mathematically that from the first to the eleventh decade arterial extensibility decreases quite rapidly. The elasticity of veins varies and also diminishes progressively with age. From the figures in Table 2 it is manifest that careful evaluation and study of the cardiovascular system is of prime importance in senescent urologic disease. Pulmonary diseases also are major complicating *factors*.

From a urologic standpoint, concurrent circulatory system abnormalities or incidents accounted for nine of nineteen deaths following operation (see Table 3). Of the entire group, eighty-nine suffered abnormally high blood pressure and seventy presented evidence of heart disease. Thus, we are convinced that diseases of the heart and blood vessels are the most important considerations in a physiological urologic inventory. Arising of the vascular tree in older people usually almost inevitably results in arterial sclerosis with varying degrees of renal atrophy and connective tissue proliferation. Fortunately, under normal senescent circumstances polyuria develops, counteracting or counterbalancing the distortion of the urinary concentrating mechanism.

The body as a whole has an inherent physiological or biological reserve

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which as a rule comes immediately to the fore when stresses and strains develop As an individual grows older this reserve diminishes, but it is never completely exhausted until death Such a fact is comforting but it is, alas, impossible to estimate accurately this so-called "reserve" Therefore, any surgical procedure in a patient old physiologically, despite the given age, or truly patriarchal by reason of years lived, must be

TABLE 1

AGE GROUPS

Age	Number	Age	Number	Age	Number	Age	Number	Age	Number
70	10	75	6	80	3	85	2	90	2
71	12	76	13	81	4	86	0	96	1
72	11	77	9	82	2	87	4		
73	11	78	7	83	3	88	1		
74	12	79	3	84	3	89	0		
70–74	65	75–79	38	80–84	15	85–89	7	90–96	3

Total	128
Average age	75 5%

TABLE 2

COMPLICATING COINCIDENT MEDICAL DISEASES

		Total
Hypertension		89
Above 150/90	50	
Above 160/95	39	
Cardiacs		70
Decompensated	14	
Severe	24	
Mild	32	
Arthritis		14
Pulmonary diseases		12
Anemias		12
Diabetes		6
Hemiplegia		5
Old cerebral accidents		4
Psychoses		4

undertaken only after careful consideration of all pertinent and relative factors

There is a marked paucity of literature as regards urologic surgical experience in age groups 70 years and over Such surgical reports as

were pertinent, for the most part concerned general surgical problems age 60 having been accepted as a base line. As such, the mortality rate was 7 to 34 per cent, increasing in almost arithmetical progression with the age increment. Our death rate from all causes for the age range 70–96 was 14.8 per cent (see Table 5, recapitulation). Speaking generally, urologic mortality rates vary from 6 to 22 per cent in open prostatic surgery and about 2 per cent in transurethral surgery for an all inclusive age ratio. A higher mortality rate prevails throughout the country in so-called "county hospitals" as compared with private institutions.

Our geriatric urologic patients had a total of 136 admissions and readmissions during the two and one half year period 1945–1947, and, as stated, the age range was from 70 to 96. Inasmuch as Morrisania City Hospital is an institution for the care and treatment of the indigent poor, it follows that such a group represents, by and large, strata of minimal social and financial advantages.

Sick, old people are in many respects like infants or young children in that their ills and woes must often be diagnosed by observation, physical examination, deduction and elimination. Quite frequently because of sclerotic brain changes, they are unable to give a coherent or sensible estimate of the "present illness"—to say nothing of an intelligent or helpful "past history." Family cooperation, therefore, is of prime importance, and not infrequently information gleaned from a wife, a son, a daughter, or even a friend, may be of great value in the treatment and prognosis of an aging oldster.

Prostatic diseases accounted directly for by far the greatest number of admissions (110) in this series (Table 1). It is thus quite evident that prostatism is the most important acquired or concomitant urologic disease of aged males.

Prostatic malignancy was found in eighteen cases (14.6 per cent), complicated in one instance by concomitant polycystic kidney disease. Carcinoma of the bladder occurred in six patients or 4.6 per cent. It was uncomplicated in three, two others presented intercurrent benign prostatic hypertrophy, and one had a simultaneous bladder calculus. In one patient (female) a malignant pelvic tumor obstructed the left ureter. As such it is included in the twenty five urologic tract malignancies herewith reported (which 19.5 per cent of our series of 128 patients).

As indicated in Table 4, it is evident that our patients suffering benign prostatic hypertrophy complained of persistent urinary symptoms or disorders [illegible] in patients afflicted with prostatic cancer. In our experience, a urinary retention is not a significant [illegible] hypertrophy [illegible]

Benign hypertrophy of the prostate gland stands out for particular consideration in patients 70 years of age and over (total 92, Table 3) Malignant disease of the urinary tract is, numerically, of comparatively

TABLE 3

FINAL DIAGNOSIS

		Total
Benign prostatic hypertrophy		92
Uncomplicated	84	
Urethral stricture	1	
Vesical calculi	7	
Carcinoma of prostate		18
Uncomplicated	17	
Polycystic disease of kidney	1	
Carcinoma of the bladder		6
Uncomplicated	3	
Benign prostatic hypertrophy	2	
Vesical calculus	1	
Pelvic tumor—extrinsic urinary tract malignancy		1
Calculous pyelonephritis		2
Renal calculus		2
Pyonephrosis		1
Pyelonephritis		1
Cyst of kidney		1
Vesical calculus		1
Suprapubic cellulitis		1
Incontinence		1
Perineal fistula		1
		128

TABLE 4

DURATION OF SYMPTOMS PRIOR TO ADMISSION

(Benign Prostatic Hypertrophy and Carcinoma of the Prostate Gland)

	Number	Per Cent	Duration of Symptoms Prior to Admission, Months
Benign prostatic hypertrophy—In retention	58	63	35 3
—Able to void	34	37	24 5
Carcinoma of prostate—In retention	7	39	11 6
—Able to void	11	61	7 4

secondary importance (total 25, Table 3) but assumes a major role when we realize that seven of the nineteen deaths herewith recorded occurred in patients suffering cancer of the prostate (total 4, Table 5) and bladder (total 3, Table 5)

In Table 5 are recorded important facts concerning nineteen postoperative deaths. Twelve followed cystotomy, but these operations were of an emergency character to provide urinary drainage. All nineteen patients who died gave a history of serious preoperative medical disease. Interestingly enough, thirty-three of the 128 individual patients operated upon gave no history of preexisting disease, and not one death occurred in this group. There is no doubt in our minds, however, that simple cystotomy is, from a mortality standpoint, more dangerous than actual enucleation of the prostate gland. Our operative mortality subsequent to transurethral prostatic resection is much less than that following prostatectomy.

We consider it worthy of note that in our series of 128 patients 70 years of age and over not one suffered from a malignant disease of the urinary tract save cancer of the bladder or prostate. The inescapable conclusion derived from the figures is that victims of cancer elsewhere in the urinary tract will probably die before the seventieth year. In other words, we find that cancer of the prostate and bladder are particularly selective diseases in patients over 70 years of age.

BENIGN PROSTATIC HYPERTROPHY

Removal of an hypertrophied or obstructing prostate in a man of 70 or over will by no means decrease his apparent years nor, as a rule, restore his lost or diminished potency. If, on the other hand, he is privileged to have unusual sexual vigor prior to operation, the operation should not in the great majority of patients (80 per cent) change his preoperative sexual behavior.

An obstructing prostate is inherently of serious consequence because of the secondary degenerative changes which it may cause in the cardiorenal systems.

An aging vascular tree is in itself a liability which calls for increasingly greater demands upon the basic but coincidentally diminishing physiologic reserves of the body. Thus in the senescent a constant increase of intravesical hydrostatic pressure, sooner or later will be followed by serious renal symptoms of fluid, nitrogen and electrolyte imbalance.

Abnormally high blood urea nitrogen was noted in about 70 per cent of our patients suffering either benign prostatic hypertrophy or carcinoma of the prostate. Except in emergencies we prefer the estimation of blood urea nitrogen rather than a polycythemia determination, because of the two tests, the former is far an elevation that an earlier sign.

[illegible]

TABLE 5

ANALYSIS OF POSTOPERATIVE DEATHS

Age	Duration Symptoms	Medical Complications	Diagnosis	Operation	Anes	P O Day of Death	Cause
70	2 yrs	Card decomp	B P H *	Cystotomy	G -O -E	1	Cerebral acc
81	3 "	Cerebrovasc accident	B P H	"	"	1	" "
75	5 "	Coronary occlusion	B P H	"	"	1	Cardiac
77	1 "	Uremia, debility, pyonephrosis	Cystitis	"	Local	1	Uremia
90	2 "	Hyper cardiac, bronchitis	B P H	"	Cyclo	4	Bronchopneum
82	3 mos	Hypertension	Ca prost	"	Local	5	Pneumonia
73	2 yrs	Hyper cardiac	B P H	"	Cyclo	8	Pulm embolus
76	6 mos	Coronary dis	Ca prost	"	"	18	Coronary
77	2 yrs	Uremia	B P H	Trocar cystotomy	Local	22	Uremia, bronchopneum
74	3 "	Card Hemiplegia Cerebrovasc accident	B P H	Cystotomy	"	47	Uremia, bronchopneum
90	3 "	Nephrosclerosis Hyper cardiac	B P H	Prostatectomy	G -O -E	2	Cerebral acc
70	2 "	Hyper cardiac	B P H	Prostatectomy for bleeding	"	3	Cardiac
72	1 "	Arthritis	Ca prostate	Prostatectomy	"	19	Bronchopneum
74	1 "	Hyper cardiac	Ca prostate	Resection	Spinal	1	Cerebral acc
71	3 "	Hyper heart disease	B P H	"	"	9	Coronary throm

[illegible]	[illegible] yr	Diverticulitis [illegible]	Ca Bladder	Cystoscopy & fulguration	Spinal	2	Debility
[illegible]		Hypertension	Ca Bladder	Cystoscopy & fulguration	IV pent	3	Shock
[illegible]		Hypertension	Ca Bladder	Nephrostomy	G. O. E.	6	Uremia
[illegible]		Hypertension	Calculus pyelonephritis	Nephrectomy	Cyclo	20	Cardiac

Recapitulation—Causes of Death

Total Number of Patients		128
Cardiovascular disorder	5	
Cerebrovascular accident	4	
Pneumonia	3	
Uremia	4	
Pulmonary embolus	1	
Tuberculosis	1	
Shock	1	
Total number of deaths	19—14.8 per cent	

Hence Prostatic Hypertrophy

centrate Complete renal failure and death will follow in sequence and consequence

Thus, an accurate and prompt recognition and appreciation of the signs and symptoms, and treatment of obstructive prostatism in elderly males will materially increase their life span and enable them to live comfortable and even more productive lives

The average age of our patients was 75 5 years (Table 1) A definite decrease in the number of patients in each successive five-year group is an interesting fact, but understandable when the average age of death (65 years, plus) for the population as a whole is taken into consideration However, we did operate upon twenty-five patients over 80 years of age and but four of them died The final diagnosis in three was benign prostatic hypertrophy, and in one case, carcinoma of the prostate (Table 5) The oldest survivor was 96 and he comfortably withstood a two-

TABLE 6

ESTIMATION OF UREA NITROGEN

Urea Nitrogen	Benign Prostatic Hypertrophy	Carcinoma of Prostate
Normal	28	5
16–24	31	7
25–34	16	3
35–50	9	2
50–75	5	1
Over 75	3	
Total	64	18
Per cent	69 5	72 2

stage suprapubic prostatectomy Prostatectomy has been reported infrequently as successful in the tenth and eleventh decades

Prostatism is the most frequently encountered disease of male senescence However, it is usually possible satisfactorily and safely to control or relieve the untoward local or systemic symptomatology by surgery Naturally, it follows that the sooner prostatic obstruction is eliminated the more satisfactory the immediate and end results will be Prostatism should be carefully considered as a possibility in every male patient 40 years of age and over who complains of even slight urinary disturbances Elderly males are particularly prone to regard frequent or difficult urination as a normal consequence of advancing age because the onset is so insidiously slow and painless Fortunately the public as a whole is becoming more and more "prostate conscious" and fewer elderly or aged patients seem to have an insurmountable fear of urologic surgery Such a happy circumstance can only be due to the informative educational missionary work of medical practitioners who appreciate the potentially destructive effects of prostatic obstruction

Pathogenesis

Prostatism or bladder neck obstruction in the aged is most commonly the result of benign adenomatous hypertrophy of the prostate gland. In our operative series of 128 patients, a postoperative diagnosis of benign adenomatous hypertrophy of the prostate gland was made in ninety-two, or approximately 72 per cent (Table 9).

In this regard it is well to appreciate the fact that median bar formation and contracture of the bladder neck may cause symptoms identical with those of prostatic hypertrophy. However, such a finding is most unusual in the senescent and is usually demonstrable only in the younger age groups.

The most recent and best pathologic opinion is that intracapsular hypertrophy of the gland is the result of proliferation of glandular rests which press the component parts of the preformed prostate gland against the capsule. The enlargement is most commonly demonstrable in the lateral and median lobes of the gland. Rarely is the anterior or posterior lobe involved.

Embryologically and anatomically the subvesical glands or tubules are not part of the prostate gland but they usually proliferate or hypertrophy simultaneously with lateral and median prostatic lobes.

Symptomatology

The predominant or outstanding urinary symptoms complained of by our elderly or old patients suffering benign adenomatous prostatic hypertrophy were (*a*) frequency, (*b*) urgency, (*c*) burning, (*d*) pain, (*e*) difficult voiding (partial retention), and (*f*) retention (complete). Frequent urination was by far the most constant symptom. As a rule, this manifestation could be traced back for years, slowly but persistently increasing in severity. Diurnal frequency they all accepted as a manifestation of age and, as such, it caused them little concern. Nocturia, however, if it occurred more than five or six times after bedtime, did seem to arouse suspicion that "something was wrong."

All seemed to agree that urgency and burning were disagreeable but not important even if accompanied by dribbling. On admission many were found wearing pads of some sort to absorb the uncontrollable drops of urine.

Dysuria was a constant but was complained of sufficiently often to warrant its inclusion as a major symptom. More frequently than not the pain complained of was in the region of the glans penis and usually followed the act of micturition.

[illegible] years the elderly urologic patients previously suffered but were

always hopeful that the situation would right itself—which it never did Ultimately, having frequently spent ten to twenty minutes or even longer attempting to void, and in the end being rewarded by the passage of perhaps only a few cubic centimeters of urine, the situation became intolerable

Repeated episodes of acute urinary retention eventually resulted in hospitalization However, one such experience, in the great majority of instances, usually caused an emergent call for the ambulance

Of our 110 patients suffering prostatism, thirty-four, or thirty-seven per cent, were able to void but with untoward accompanying symptoms, and fifty-eight, or sixty-three per cent, were in a state of acute or chronic retention of urine All gave a history of having suffered from two to about three years prior to admission

Diagnosis

The diagnosis of senescent prostatism in a conscious patient is not difficult as a rule, particularly if due attention is given a past or present history of abnormal urinary symptomatology (*v s*) and if upon digital rectal examination an enlargement of the gland is found All aged patients proven to have or even suspected of having prostatic glandular hypertrophy should be instrumentally examined most gently and only under aseptic conditions The passage of even a soft rubber catheter may cause surgical shock or result in kidney failure and anuria However, if, with a significant past history and prostatic hypertrophy the catheter frees a large quantity of urine, or even a small amount, which the patient is unable to voluntarily void (residual urine), a diagnosis of prostatism is further justified An x-ray film of the urinary tract may be helpful as regards coexisting abnormalities such as stone Of course, if an elderly or senescent patient is unconscious or semiconscious on admission, the diagnosis of prostatism must be guarded even if an enlarged prostate is discovered Brain and cord injury or disease, cerebral accident, diabetes and nephritis (uremia) must all be given pertinent consideration Consequently, the necessity for cooperation of medical, surgical and urologic services is imperative

Treatment

Preoperative Treatment—Proper and adequate preoperative treatment of the senescent urologic patient presupposes the close cooperation of the internist and urologist Coincidental medical diseases are frequently of such severity and import that only emergent surgery can or should be contemplated The opinion of the medical consultant is our criterion for optimum preoperative condition of the patient Prostatic obstruction always places an added burden upon the heart by reason of

nocturia, with concomitant loss of sleep and rest. Cardiac decompensation, save in emergency, is a positive contraindication for urologic surgery. The study of the urinary system, per se, prior to operation is an inadequate preparatory measure. The entire physiological picture must be properly evaluated.

A patient on the borderline of renal compensation can easily be pushed into a serious state by secondary factors. A vicious cycle may develop. Decreased cardiac function diminishes renal function. Alterations in the fluid and electrolyte balance has a deleterious effect upon the heart. Consequently such a cycle must be broken. Prompt drainage of the bladder is usually the answer.

It must be admitted that a relatively high mortality is commonly expected in the older age groups, but death directly attributable to surgery is remarkably infrequent. The total number of deaths which we herewith report is nineteen, or 14.8 per cent (Table 5).

The majority of our patients had more than one coincident medical disease. A combination of diabetes, hypertension, arteriosclerosis and arthritis was not uncommon.

The importance of the recognition and treatment of cardiovascular diseases in senescent urologic patients cannot be overemphasized. Thirty-eight of our patients had severe cardiac disease and thirty-two manifested comparable but milder signs and symptoms. Thus, at least 55 per cent of the total (128) required carefully considered preoperative medical treatment. Willius reported a series of cases in which 42 per cent of those suffering benign prostatic hypertrophy had cardiovascular disease.

Since the great majority of our severe cardiacs had coincidental renal decompensation, mercurial diuretics were not used. Digitalis was the drug of choice. Twelve patients had hemoglobin readings below 10.5 gm. Transfusions of citrated blood were given, preoperatively, slowly, if the anemia was marked. Various iron and vitamin preparations were also administered when indicated.

A negative nitrogen balance and protein depletion must be corrected. Therefore plasma proteins or amino acids were cautiously administered intravenously. Care must be taken in injecting such fluids parenterally in the treatment of azotemic or uremic patients because it is easy to completely overwhelm already damaged kidneys.

Twelve patients suffered from no pulmonary disease but except for the anesthetic problem they presented no unusual problem. Most of the arthritic patients suffered typical symptoms of spinal involvement but tests were simply for free and the arthritic conditions were discovered by x-ray examination alone.

We have not [illegible] that the urologic senescent patient will be

a much better risk if surgical measures can be delayed until (*a*) cardiac compensation is obtained, (*b*) diabetes is controlled, (*c*) acid base balance is normal, (*d*) blood urea nitrogen is stabilized, (*e*) hemoglobin is normal, (*f*) nutritional state is properly restored, and (*g*) the bladder is slowly decompressed All factors except the last are primarily medical problems

Decompression of Urinary Bladder—For elderly patients suffering acute or chronic urinary retention, slow decompression of the bladder is axiomatic If the retained urine is gradually removed there will be much less chance of serious hemorrhage from the mucous membrane of the bladder or complete suppression of urine because of kidney failure Both of these untoward eventualities usually are due to too rapid decrease in the hydrostatic pressure of the urinary system Decompression of the bladder is best accomplished by an indwelling catheter to which is attached two appropriate lengths of rubber tubing A straight glass connecting tube connects the first length to the catheter and an *inverted* glass "Y" unites it with the second length The *inverted* "Y" tube should then be secured to an upright standard on a firm base, at the level at which the retained urine is first observed to flow into the second or dependent length of tubing By lowering the inverted "Y" tube about 1 inch a day until it is level with the tuberosity of the ischium the urinary bladder will be safely decompressed If a patient presents over 75 or 100 cc following a normal effort to void, gradual urinary decompression should be instituted prior to an operative procedure Suprapubic trocar cystotomy may be performed and adapted for urinary decompression It should be used only when simpler methods fail

The Catheter—Relief of discomfort or pain coincidental with acute or chronic urinary retention is paramount Fortunately, such relief is frequently afforded by the passage of a soft rubber catheter Trauma of the urethra even in young people may be followed by most unpleasant consequences Severe chill, shock and hemorrhage are the most common untoward sequelae Any instrumentation of the urethra, particularly in elderly or old patients, must be accomplished most gently and aseptically No anesthetic should be used for the passage of a catheter because serious damage to the delicate membranes may occur without being recognized If urethral bleeding follows the passage of any type of instrument, a local anesthetic of any kind to the urethra is positively contraindicated, for the drug may be directly introduced into the blood stream with disastrous results If a soft rubber catheter fails to pass following careful and persistent effort, a mild sedative may prove helpful in allaying the patient's fear and apprehension Sodium luminal 0 06 mg hypodermically, seconal 0 09 mg by mouth, or another barbiturate is appropriate Subsequently, the various silk-woven catheters and filiforms

should be tried. Gentleness is the watchword, but the pressure must be relieved in one way or another.

Cystoscopy and Radiography.—A complete cystoscopic examination of an old or elderly patient is a serious procedure and should not be performed until the best advices of an internist have been obtained and considered.

In patients suffering prostatism, accurate preoperative information concerning the upper and lower urinary tracts is of great advantage. No operation on the urinary tract, except in an emergency, should be performed until the patient has been examined cystoscopically and radiographically. The cystoscope is a potentially dangerous instrument even in skilled hands, but it will show pathologic changes in the lower urinary tract—particularly of the prostate gland, bladder and urethra. Digital palpation of the gland cannot be relied upon to decide the appropriate type of operation for the relief of prostatism. Particularly in the senescent, transurethral cystoscopic resection of the prostate gland is the safest of all surgical measures for the ablation of prostatic obstruction. In this regard only cystoscopy can give the information necessary for an accurate, intelligent decision as regards the type of operation which should be performed.

General anesthesia for a cystoscopic examination of a senescent patient is rarely indicated. Provided proper preoperative sedation has been given, local anesthesia is as a rule quite satisfactory. At times caudal anesthesia may be most appropriate. The examination should be performed as gently and painlessly as is possible. Speed is not a prerequisite for cystoscopy, but dawdling and unnecessary delay are inexcusable.

Kidney function is of great import as regards prognosis. The blood urea may prove to be within or near normal limits and the phenosulfonephthalein excretion may be more or less satisfactory, but such tests will not determine whether one or both kidneys are functioning. The passage of a ureteral catheter via the cystoscope to the pelvis of each kidney will ultimately give the most reliable answer.

Upper urinary tract disease may not be clinically evident, but retrograde or intravenous pyelography will show otherwise unsuspected conditions which may change the whole picture as regards prognosis and treatment. Of the two radiographic methods, retrograde pyelography is the more accurate. However, if for some good reason this procedure cannot be carried out, then intravenous urography is invaluable. It may be well to bear in mind that if the blood urea is over 50 mg., good excretion of the contrast medium which has been injected intravenously cannot be expected and unsatisfactory films will result. Incidentally, we do not believe that excretion urography is an accurate index to kidney

function We rely chiefly upon the quantitative estimation of phenosulfonephthalein in specimens of urine collected from each kidney by means of the ureteral catheters Cystourethrography may demonstrate defects or disease of the bladder and entire urethra which the cystoscopy cannot evaluate Faulty technic in this regard, however, may result in unreadable or misleading films

Operative Treatment.—Old age should not, per se, be considered a contraindication for surgery, but even now we cannot exchange physiologically old lamps for new Consequently, the purpose of geriatric urologic surgery is restoration of the patient to a status considered normal for his age group

Many days, weeks or even months may be necessary for the adequate conditioning of a senescent patient for a major surgical operation, particularly the second stage of suprapubic prostatectomy The resiliency and adaptability of the tissues is reduced as the years advance As a rule, the cardiovascular system, especially the myocardium, has been impaired in the physiological process of living and has little reserve in an emergency The arteries are less resilient Surgical shock, once it has developed in a senescent patient, is more difficult to reverse than in a vigorously mature patient Fluids should be given neither rapidly nor in great quantity Stimulants and sedatives or hypnotics must be administered cautiously The senescent patient reacts most unfavorably to loss of blood and extremes of temperature, particularly cold For such an individual, the prognosis of a major urologic surgical operation must be based upon an appreciation of the probable life expectancy and a properly evaluated physiological inventory

Major urologic surgery in the aged is indicated for (*a*) relief of pain, (*b*) restoration of maximum possible function to already damaged organs, (*c*) removal of obstruction to urinary output, (*d*) excision or control of cancer, and (*e*) relief of infection

Urologic surgery in the older age group of patients should be performed only by well-seasoned, capable and competent surgeons To quote Franken, "the surgeon must act with speed without losing accuracy, with discretion without undue neglect of essentials and with gentleness so as to protect the fragile tissues of his aged patients " Attention to minute details, hemostasis and adequate repair of tissues must be stressed

Anesthesia for Major Urologic Surgical Operations —Anesthesia for old people is a serious problem The combined judgments of internest, anesthetist and surgeon should determine the choice of anesthetic By and large, intravenous pentothal sodium should not be used Local anesthesia is perhaps the safest of all methods, but unfortunately it is not always indicated or practicable Any

closed anesthetic sequence should have a high oxygen content. Spinal anesthesia may well be the method of choice.

Preoperative sedation is of great importance because it greatly facilitates the administration of the anesthetic and allays the fear on the part of the patient regarding the proposed surgical procedure. Morphine is contraindicated as a sedative for patients over 70 years of age. It causes excessive depression of physiological functions. Small doses of the barbiturates should be used.

Two hundred twenty six anesthesias were given (Table 7) with but one important complication—auricular fibrillation—on the operating table. In this case, when ether was promptly substituted for the first anesthetic, cyclopropane, fibrillation stopped and no untoward results followed. There were no so-called "anesthetic deaths." When parenteral fluids were given during an operation 60 to 70 drops per minute was the maximum rate. Dillon does not recommend spinal anesthesia when the hemoglobin is below 12 gm. or the systolic pressure over 180 mm. of mercury. Our anesthesiologist followed his advice.

Lawrence, reviewing a series of operative results from an anesthetic standpoint, found the normal male under 60 years of age tolerated satisfactorily 100

TABLE 7

ANESTHESIA (MAJOR OPERATIONS)

Intravenous pentothal	9
Local	37
Cyclopropane	60
Gas-oxygen-ether	65
Spinal	54
Caudal	1
Total	226

minutes of anesthesia in prostatic surgery. Above age 60 he reported a mortality rate of 24 per cent when the anesthesia and surgery were continued more than eighty minutes.

In all these patients the circulatory system has already been depleted of compensatory mechanisms. The respiratory system as a rule reveals a reduced vital capacity and frequently an impairment of the oxygen-carbon dioxide exchange [illegible].

Anesthesia [illegible] properly [illegible] assumed its important and proper place as a specialty. [illegible] well trained cooperative anesthesiologist [illegible] totally necessary for the proper [illegible] of urologic surgery. The [illegible] clearly define the immediate [illegible] of the patient. The [illegible] legally [illegible] the potential [illegible] [illegible] [illegible] with [illegible]

[illegible] There are few reasons [illegible] method [illegible] [illegible]

(a) suprapubic prostatectomy, (b) perineal prostatectomy, (c) retropubic prostatectomy and (d) transurethral cystoscopic resection The method of choice depends upon (a) the type of prostatic enlargement or disease and (b) the operator's disposition, training and experience

Urologic surgeons should be familiar and experienced in all four methods and perform the operation which in their hands and under similar circumstances has given them and the patient the most satisfactory results No one method is universally applicable to all types of prostatic hypertrophy and bladder neck obstruction Generally speaking, suprapubic prostatectomy is preferable if the hypertrophy is intravesical, perineal section for extravesical enlargement, and transurethral resection in contracture of the bladder neck, median bar formation

TABLE 8

MAJOR OPERATIONS

Second stage prostatectomy	57
One stage prostatectomy	2
Perineal prostatectomy	1
Transurethral resection	38
Trocar cystotomy	7
Cystotomy	78
Cystotomy, removal of vesical calculi	8
Cystotomy with fulguration	3
Secondary cystotomy	1
Tertiary cystotomy	1
Secondary closure of cystotomy	1
Orchiectomy	12
Epididymotomy	2
External urethrotomy	2
Internal and External urethrotomy	1
Plication of external urethra	1
Subtotal bladder resection	1
Nephrectomy	5
Nephrostomy	3
Nephrolithotomy	1
Excision of cyst, upper pole of kidney	1
Total	226

and median and lateral lobe enlargements Retropubic prostatectomy, as reintroduced and modified by Millan, should presumably give satisfactory end results for either intra- or extravesical prostatic hypertrophy We have not deemed this operation appropriate in this series of patients 70 years of age and over because of the possibility of intercurrent operative hemorrhage For the younger age groups, however, our end results have been encouraging

We are rather inclined to favor suprapubic enucleation of the gland in the majority of senescent patients suffering prostatism, and performed this operation upon fifty-seven patients Perineal prostatectomy was deemed advisable for one and transurethral prostatic resection was performed thirty-eight times on thirty-six patients

Postoperative Treatment.—In our experience the two-stage suprapubic prostatectomy has given best results. The interval between the two stages varied from eight days to four months. Six patients were discharged following cystotomy with their suprapubic tubes in situ to convalesce elsewhere. They were all severe cardiacs and it was felt that if they were given ample time to recuperate under careful medical supervision the ultimate removal of the prostate gland would be less of a hazard. Three were readmitted and the gland was enucleated with no deaths. Three were readmitted but were considered inoperable even after rest and excellent medical care and treatment. They were discharged to finish their days in comfort with adequate suprapubic drainage of the bladder. Permanent suprapubic drainage may enable many old men to live their lives in comfort. However, not infrequently an indwelling suprapubic catheter may restore the function of the kidneys to such an extent that a subsequent prostatectomy will prove feasible. Urethral catheter drainage will provide equally good results, but unfortunately the urethra resents the foreign body after a time and it must be removed. Proper use of the antibiotics and sulfonamides will prolong catheter tolerance.

The elderly patient should be kept warm—heaters and blankets are usually essential to the maintenance of proper body temperature. The continuance and regulation of intravenous fluids started on the operating table must be maintained when the patient has been returned to his bed. Should the blood loss be deemed excessive or a concurrent but unexpected infectious process be discovered during the operation, transfusion(s) of whole blood in small amounts, is in order. Vitamins B and C are most helpful, as is a high protein diet. If food is not tolerated, intravenous proteins—hydrolysates and amino acids—should be prescribed in proper quantity by the consulting internist. Fluid intake and output should be carefully recorded and evaluated. A careful check of the electrolyte balance is also important.

A convalescent patient should be encouraged to get out of bed promptly. Early ambulation will prevent many pulmonary and arteriovenous disasters. Naturally due consideration must be given any underlying circulatory deficiency—to quote the internist. Operative wounds in old people usually are slow to heal. Their muscles are flabby and the fascial layers are thin and weak, but moderate exercise will be helpful. Many an elderly patient died because she was kept in bed too long.

CANCER OF THE PROSTATE GLAND

Cancer of the prostate gland is much more frequent in the older men and women. It is well to remember that almost 15 per cent

of all patients complaining of symptoms of prostatism may have cancer of the prostate gland

The premonitory symptoms of prostatic cancer in our senescent patients were of much shorter duration than those of benign hypertrophic prostatic adenoma (Table 4), but otherwise they are identical Consequently, any elderly patient suffering from prostatism should, in all fairness, be suspected of harboring malignancy If such a gloomy attitude is assumed and taken advantage of, the earlier will be the discovery of prostatic cancer and its amelioration or possible cure

To date we must admit that cancer of the prostate gland is not radiosensitive and does not respond satisfactorily to x-ray therapy Furthermore, an old man may complain of no other symptoms of prostatism than lower back pain or "sciatica" Nevertheless, malignancy of the prostate gland should be considered

Cancer of the prostate as a rule originates in the posterior lobe of the gland and therefore does not usually cause early symptoms of urinary obstruction, such as urgent and frequent urination Cancer may originate in any of the other four lobes of the gland Not infrequently the diagnosis of prostatic cancer is, surprisingly and primarily, made by the pathologist who has carefully examined sections of the prostate gland removed at operation in which the disease was not diagnosed or suspected

Diagnosis—If, upon digital examination of the prostate gland, an area of induration or nodulation is discovered, cancer of the gland must be suspected This is a fact whether the patient be young or old

Tuberculosis of the prostate may be hard to differentiate by rectal examination, but it is, practically speaking, never a primary disease, especially in the senescent Biopsy of the suspected area is imperative for an accurate diagnosis This may be accomplished in two ways—(*a*) by perineal biopsy (trocar), or (*b*) by transurethral resection Of the two, perineal biopsy is the less hazardous Naturally, if the obtained specimen of tissue is reported malignant, that is the answer However, a negative pathological report of the biopsy specimen obtained by either method is not conclusive evidence of a noncancerous prostate It is only too easy for the surgeon to miss the critical area when taking the specimen

How early bony metastases occur is not known, but the blood supply of the prostate gland is directly connected with the lumbar vertebrae and the ilia Consequently, an early bony extension of the disease may well be expected

Any bony abnormalities demonstrated by x-ray when cancer of the prostate is suspected must be seriously considered However, the presence of metastatic malignant bone disease is not indicative of prostatic cancer even if the lumbar vertebrae and ilia are involved

The determination of acid and alkaline phosphatase in blood serum provides important contributory evidence. Usually carcinoma of the prostate is accompanied by an increase of acid phosphatase, but this is not always so. Some studies postulate that, when bony metastases are evident in patients suffering malignant disease of the prostate, an increase of alkaline serum phosphatase is present, but this is not always so. Many factors such as the personal constancy and ability of the laboratory technician enter the picture so that an increase or decrease of the blood phosphatase movement must be correlated with the clinical findings before an accurate diagnosis can be established.

Treatment.—There is no specific treatment for carcinoma of the prostate gland. Urinary retention, however, must be relieved and the relief is usually best accomplished by an indwelling catheter. Following a period of urethral catheter drainage if the patient is unable to void, orchiectomy is recommended because bilateral orchiectomy in elderly patients almost invariably is accompanied by shrinkage of the gland. Even so an occasional patient cannot void. In such event transurethral cystoscopic resection of the obstructive portion of the prostate is necessary and usually helpful. However, the less instrumentation, the less manipulation and the least surgery a malignant prostate gland is subjected to the better off the patient will be.

Estrogens, in appropriate doses, may give satisfactory palliative results. We believe that a combination of therapies accomplishes the best end results: bilateral orchiectomy plus estrogens. The individual reaction of the patient to hormones administered orally cannot be determined except by trial and error. Ordinarily, 0.05 mg. of diethylstilbestrol three times a day will cause no untoward symptoms. For best results we think the drug should be given to the point of maximum individual tolerance. If the diagnosis of prostatic cancer can be established before extension through the capsule occurs, perhaps total prostatectomy may be found otherwise to. Hormonal therapy and bilateral orchiectomy, except in rare instances, is not considered to be curative in cancer of the prostate. If such modalities are properly employed, however, death, although ultimate, will be postponed and much less painful for the patient and for the family.

In our series of 188 patients, we diagnosed carcinoma of the prostate in [illegible] or 14.8 percent of the total admissions (Table 1). Bilateral orchiectomy was performed in [illegible] of these patients, [illegible] refused the operation. Four patients died [illegible] after the relief of prostatic [illegible]. The death of [illegible] was due to [illegible] after prostatectomy from [illegible] hemorrhage and [illegible]. The death rate was [illegible] percent.

The same preoperative and postoperative principles and practices were followed in patients suffering malignant prostatism as has been described under the heading "benign prostatic hypertrophy"

Most of our postoperative complications (Table 9) followed enucleation of the prostate gland (35 per cent) Difficulties as the result of transurethral resection occurred in about 10 per cent

TABLE 9

POSTOPERATIVE COMPLICATIONS

Total Cases	Prostatic Enucleation 60	Transurethral Resection 38	Others 128
Bronchopneumonia	4	0	5
Bacteremia	1	0	0
Cardiac failure	1	1	3
Cerebral accident	3	1	2
Epididymitis	8	0	0
Infected wound	2	0	1
Phlebitis	1	1	0
Psychosis	1	1	0
Pulmonary embolism	0	0	1
Shock	0	0	1
Toxemia	0	0	1
Total	21	4	14
Per cent	35	10 5	10 9

CANCER OF THE BLADDER

Six of our senescent patients suffered from malignant disease of the bladder and all were operated upon (Table 3) One is alive at the present time and is enjoying life comfortably, five are dead Three died postoperatively in the hospital (Table 5) and the other two at home about six months after operation

Of all the body neoplasms, cancer of the bladder is one of the least frequently encountered Very few deaths occur from this cause in individuals under 25 years of age The death rate from cancer of the bladder rises continuously with advancing years

Diagnosis.—The first objective evidence of bladder tumor is hematuria, painless or otherwise The diagnosis of vesical neoplasm can best be made at the time of cystoscopic examination As a matter of fact, we are more inclined to rely upon visualization of a bladder lesion for the diagnosis of malignancy than upon examination of the biopsy specimen Very often a biopsy report may be misleading, particularly if "negative for malignancy" We are reasonably positive that all bladder tumors either are actually or potentially malignant

Treatment —The treatment of bladder tumors is primarily surgical The growth should be destroyed or removed, if possible Many methods are recognized for the accomplishment of this purpose Deep x-ray Treatment is practically valueless The use of radium implantations may be of value in a small proportion of cases At the present time there is no treatment that will give uniformly satisfactory results Some malignancies prove intractable to any and all forms of treatment In elderly patients particularly, an early diagnosis provides the best opportunity for effective therapy Whereas in young or middle aged patients radical surgery may be well withstood a senescent individual under similar circumstances may not survive Diversion of the urinary stream either by suprapubic cystotomy, transplantation of the ureters to the skin or bowel or nephrostomy may be the only way in which an old man's life may be prolonged or made comfortable

The principles of preoperative and postoperative handling of the senescent patient which have already been discussed in connection with benign prostatic hypertrophy are equally applicable to patients suffering from cancer of the bladder

COMMENT

As can be seen, this presentation primarily intends to emphasize the frequency of prostatism as the most important urologic disease in senescent patients We also indicate that comprehensive medical care, preoperative and postoperative is vital for good end results, and that such good end results are impossible unless there is cooperation of all services on the behalf of patients in this category

OPTIMISM AND THE TREATMENT OF DIABETES TODAY

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Definition.—At a time when a pessimistic belief is being expressed in the unavoidable and inevitable development of early degenerative complications such as retinitis, arteriosclerotic nephritis, hypertension and coronary disease in all diabetic patients, regardless of the nature of treatment, it is well to inquire as to the real basis for such a belief. Realism in the philosophical sense holds that the existence of things in no sense depends on their being known. Plato, the idealist, was also the founder of a school of thought which later became realism. Facts may be true even though they have not been perceived or correctly interpreted by the individual student. In presenting certain facts we do not maintain in the phrase made famous by Leibnitz that "Diabetes is the best of all possible diseases," but rather that the treatment of diabetes, when properly applied, is good, and that its results can be made better.

THE NATURE OF DIABETES

The clinical character of diabetes is well known even though the basic cause may be obscure. Diabetes is hyposulinism, whether produced by actual destruction of the islets of Langerhans or by an interference with the action of insulin provided by insulin antagonistic substances derived from other endocrine glands or from unknown sources. Thus far, diabetes has been produced experimentally by four methods and a fifth was reported last year by Griffith:[1]

1. Removal of at least nine-tenths of the pancreas.
2. Injections of anterior pituitary extracts.
3. Injections of alloxan (in many animals).
4. Injections of glucose solution intraperitoneally, producing hyperglycemia.
5. Injection of uric acid into rabbits, producing hyperglycemia lasting several days if the rabbit had been subjected previously to a diet deficient in anthranilic acid, with resultant lowering of the blood glutathione level.

The first four methods of producing diabetes are associated either with

[illegible]

[illegible]

[illegible]

[illegible]

the destruction of the islands of Langerhans or with their actual surgical removal Best showed that a decline in insulin content may occur before pathologic change is demonstrated by present technics As yet no pathologic evidence is available for the fifth method of Griffith, so we do not know whether the hyperglycemia associated with uric acid injections results in necrosis of the islands of Langerhans

The important facts brought out in these experiments apply both to the treatment of diabetes and to its prevention Thus, if the animals are fasting, or are receiving insulin, then the injections of anterior pituitary extract fail to cause diabetes In Lukens' experiments it is observed that the administration of insulin, not long after production of damage in the islands of Langerhans, permitted actual regeneration of the islands so that the animal's pancreas showed a return to normal when examined by pathologic technics Many physicians have observed the remission of diabetes for long periods of time when insulin administration was begun soon after the onset of diabetes If hyperglycemia results in strain on the islands of Langerhans and eventual degeneration, then the treatment of diabetes clinically should have as one of its main objectives the use of diet and insulin in such a fashion as to control hyperglycemia

Unfortunately, at present the real date of onset of clinical diabetes is often unknown because of the lateness of diagnosis and the uncertainty as to the actual time of onset of the gradual reduction in the insulin reserve of the pancreas Heredity clearly underlies most of the diabetes in any community, on this hereditary tendency hinge various factors which at a certain time in life may become active enough to precipitate the disease Obesity, hyperthyroidism, hyperpituitarism and overactivity of the adrenal cortex come first to mind

Case I (32326)—A lawyer, aged 40 years, was hospitalized in March, 1948 In 1933 at the age of 25, when he applied for insurance, sugar was found in the urine and blood sugar was elevated There was no family history of diabetes mellitus At that time he had no symptoms referable to the disease, and he was treated with a "small amount of insulin for one month" and given a diet His weight at that time was 198 pounds, clothed He felt well until 1936 when, due to "overwork," he suffered a "nervous breakdown " At that time the diabetes was again investigated, and he was placed on a high protein, low fat, low carbohydrate diet and no insulin was given Over the next ten years body weight gradually declined to 150 pounds, and in August, 1947, he first became aware of blurring anf fuzziness of vision Examination revealed diabetic retinitis, and he was started on rutin, ascorbic acid and potassium iodide In March, 1948, he was referred to the New England Deaconess Hospital for further treatment On physical examination the patient was found to be well-developed and well-nourished, with a blood pressure of 180/92 The eye grounds showed extensive retinopathy of the diabetic type, the heart, lungs and abdomen were not remarkable The reflexes were physiological and there was good pulsation of the

dorsalis pedis vessels. The fasting blood sugar was 172 mg. per 100 cc., nonprotein nitrogen 40. The urine had a specific gravity of 1.020, albumin 630 mg., sugar 0.9 per cent, occasional hyaline casts, two to four red blood cells and eight to ten white blood cells per high power field. There was no anemia, hemoglobin was 14.5 gm., and cholesterol 152 mg. per 100 cc. Kidney function test showed 41 per cent of normal urea clearance and phenolsulfonphthalein excretion of 12 per cent in three hours. During the three weeks' hospitalization the diabetes was brought under control very easily by 10 units of protamine zinc insulin daily. He was placed on a diet containing 200 gm. of carbohydrate, 60 gm. of protein, and 88 gm. of fat. One week after he was hospitalized the nonprotein nitrogen was recorded as 72 mg. per 100 cc.; however, at discharge it was 46 mg. per 100 cc. During his hospital stay his blood pressure fell to 184/74. The albumin fluctuated between 0 and 280 mg. per 100 cc. The administration of rutin was continued. Capillary fragility was found to be 4 by our method, which was not an elevated value. The electrocardiogram was normal. Intravenous pyelography revealed no abnormality, but x-rays revealed calcification of the pelvic vessels and marked calcification of the tibial arteries bilaterally. He was discharged on a diet of 221 gm. carbohydrate, 78 gm. protein, and 95 gm. fat, with 12 units of protamine zinc insulin. Despite the obvious renal involvement and pronounced arteriosclerotic complications, vision and renal function have improved since inauguration of insulin treatment and a proper diabetic diet.

This case illustrates the unfortunate results of a long-continued inadequate diet with great weight loss, in the effort to avoid the use of insulin.

Case II (32589). — A 55 year old white man, first admitted to the New England Deaconess Hospital in February, 1948, had always been in excellent health, having had one illness, pneumonia, ten years before. He had "always been overweight." At the age of 20 he weighed approximately 180 pounds, clothed. Through excessive dietary intake his weight had gradually increased to 230 pounds in 1938 when he was 45 years old. Though his appetite remained good his weight declined in seven years to 170 pounds in August, 1947, when he first complained of polyuria and polydipsia [illegible] thereafter of excessive fatigue and lameness of the right leg. With the onset of cold weather his right leg below the knee was at times uncomfortably cold. Calluses which had been present on his feet for a number of years had tended to become blistered two months before admission. The first week of January, 1948, a linear crack appeared in a [illegible] his right foot [illegible] was no association of pain. The physician [illegible] blood sugar was [illegible] became sugar free in three weeks [illegible] No further urine examinations were made. He was [illegible] the New England [illegible] his weight was 154 pounds, clothed. [illegible]

tion of the heart, lungs and abdomen was negative Both fundi revealed a moderate number of punctate hemorrhages and waxy exudates No pulsation was palpable below the femoral pulsation in the right leg, the dorsalis pedis pulsation was absent in the left The right foot was cold, with extensive soft tissue necrosis involving the great toe, the first metatarsal area and the medial plantar aspect, and there were several deep fissures on the heel X-ray examination revealed extensive calcification of the vessels of the legs, but no osteomyelitis The hemoglobin was 15 gm , and the white blood count 10,300 Examination of the urine showed specific gravity of 1 025, reaction alkaline, albumin 39 mg per 100 cc , which subsequently cleared, sugar 1 6 per cent, and four to six white blood cells per high power field The blood sugar was 366 mg per 100 cc , nonprotein nitrogen 35, total protein 6 2 gm , albumin globulin ratio 1 5, and capillary fragility index 300 The patient was placed on a diabetic diet and immediately started on insulin Sixty milligrams of rutin was given four times a day, and 400,000 units of penicillin was given daily The diabetes responded well, the fasting blood sugar being 121 mg on the third hospital day Because of extensive gangrene and necrosis of the right foot, a right mid-thigh amputation was carried out on the seventh hospital day The postoperative course was uneventful On March 22, 1948, the patient was discharged walking on a temporary leg The diet contained 168 gm carbohydrate, 85 gm protein, and 98 gm fat, with 24 units of protamine zinc insulin daily

In this case, which is but one of many such tragic examples, mild diabetes had been allowed to go undiscovered for at least seven years When the diagnosis was made, treatment was inadequate because the diabetes was considered "mild " The word "mild" should rarely be applied to diabetes in middle life , it begets carelessness and neglect of treatment Actually, apparently mild diabetes may be associated with early development of malignant arteriosclerosis, gangrene, retinitis and blindness

CASE III (32540) —A 66 year old man was admitted to the N E Deaconess Hospital March 2, 1948 His father had died with diabetes at the age of 54 At 30 years of age the patient weighed 220 pounds, clothed After an attack of pneumonia, his weight fell to 190 pounds, where it remained until the early part of 1940, when, as a result of the deaths of his wife and mother and loss of his job, he became extremely upset and emotional, taking his meals at odd hours He became aware of polyuria, polydipsia and polyphagia, and he gradually began to lose weight This did not disturb him greatly, because he attributed it to his social difficulties In the meantime, he began working as manager of a bowling alley and continued until an abscess developed on the left foot in March, 1947 The diagnosis of diabetes mellitus was then established and he was placed on a diabetic diet with 6 to 8 units of regular insulin each day for one week Shortly thereafter, the ulcer healed and diet alone controlled his thirst and frequency of urination He returned to the bowling alley, working long hours and standing most of the time One night in December, 1947 when removing his sock, he noticed swelling and redness of the left great toe and "moisture around the nail " His foot doctor advised "electric current treatment" and warm soaks and he was

allowed to continue work The lesion gradually became worse On February 28, 1948, he noticed some pain in the left foot and found the left great toe to be black, with redness and swelling around the base of the toe Physical examination revealed a poorly nourished white man with blood pressure of 120/80 Both fundi showed waxy exudates with a moderate number of punctate hemorrhages with one fairly large area of hemorrhage in the right fundus Arteriosclerosis was grade 3 The heart, lungs and abdomen were not remarkable The dorsalis pedis pulsations were absent bilaterally There was dry, black gangrenous degeneration of the left great toe with swelling, redness and tenderness at the base of the toe and extending up onto the dorsum of the foot X-ray revealed calcification in the vessels of the left foot, a small amount of gas in the subcutaneous soft tissues and osteomyelitis of the terminal phalanx of the left great toe The capillary fragility index was 60 and the fasting blood sugar 188 mg per 100 cc, nonprotein nitrogen 34, hemoglobin 11 gm, red blood count 3,000,000 Examination of the urine showed 0.6 per cent sugar, one to three white blood cells Cholesterol was 162 mg per 100 cc Penicillin was started 480,000 units a day, and the foot was treated conservatively Diabetes was immediately brought under control by means of diet and small amounts of regular and protamine zinc insulin Blood sugar values leveled off, and ultimately only 8-10 units of protamine zinc insulin was required daily to control the previously elevated blood sugar The gangrenous part thus stabilized itself and on the twenty-fourth hospital day a left transmetatarsal amputation was performed The postoperative course was uneventful, the operative site healed well and the patient was started on Buerger exercises He was discharged on April 10, 1948 on a diet of 108 gm carbohydrate, 94 gm protein and 103 gm fat The blood sugar values were within normal range on 8 units of protamine zinc insulin daily The patient was walking without difficulty

In this instance symptoms of diabetes appeared in an elderly man eight years before amputation was deemed necessary One year before surgery, the diagnosis was established but here again it was considered to be mild diabetes which responded very easily to diet and small amounts of insulin and the patient's recuperative powers were such that an abscess healed with little difficulty In the year after establishment of diagnosis his diet was restricted just enough to control the disturbing symptoms of polyuria and polydipsia and the malignant phase which had already begun was allowed to run its degenerative course practically unrestrained

The Diabetes Exhibit at the annual meeting of the American Medical Association in June 1948 presented a comparison of a group of diabetic patients who had received careful examination and treatment so early that no physical or pathological complications had developed with another group of patients who came for first examination eleven or more years after the onset of diabetes when physical and pathological complications had already occurred [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible]

before complications had developed has been only one-third that in the group of patients in whom complications had already occurred Another important point revealed in this series of data is that patients who appeared for treatment in the period 1925–1929 showed a death rate three times as great as those who first came for treatment in the period 1939–1945 It is evident therefore that treatment itself has markedly improved as years have gone by Most important of all, diabetic patients whose diabetes is discovered early have a much greater chance of long life than have those whose diabetes is not discovered until complications take them to the physician

Severe diabetes always begins as a mild case, but it does not follow that mild cases must progress through the moderate to the severe stage It is largely the lack of any treatment or the improper use of insulin, diet and exercise which causes the progression of the disease Therefore, find the undiagnosed cases as well as the untreated diagnosed cases and institute aggressive treatment Realism bids us remember that the mild case seen today may be the gangrene, or carbuncle, or coma case of tomorrow!

IMPORTANCE OF EARLY DIAGNOSIS

If it were possible to discover the onset of diabetes earlier and therefore begin the use of insulin and proper diet sooner, obviously not only would the prevention of disasters such as coma, gangrene and carbuncle in previously unrecognized cases be possible, but the postponement of the premature degenerative complications would be more general

Diagnosis depends on persistent hyperglycemia and glycosuria Surveys of population indicate that in the United States probably 2,000,000 cases now exist (3,873,000 persons will have it before death)

Classification as to severity may be considered as follows

Mild cases—free from sugar with no insulin or a diet of 200 gm of carbohydrate and 10 units of insulin

Moderate cases—no sugar with 100 gm of carbohydrate, or 10 to 20 units of insulin and 200 gm of carbohydrate

Severe cases—no sugar with 50 gm of carbohydrate, or with a diet of 150 gm of carbohydrate and 50 or more units of insulin

However, no classification is satisfactory Progression from the mild to severe stage is due usually to lack of treatment Old age protects against its onset Also in diabetic families it comes on earlier in each generation, therefore, if the individual gets beyond youth, his chances of escaping diabetes improve

AIMS OF PROPER TREATMENT

Fundamentally, diet, insulin and exercise, properly combined and adjusted to the age, sex, occupation and general health of the patient,

make up the treatment of diabetes The prescribed diet should be superior to the diet in health with a view not merely toward control of the diabetic state, but also toward use of all that has been learned about nutrition in the preservation of health and avoidance of malnutrition Carbohydrate, protein and fat components should be balanced to avoid acidosis, and selected to provide the qualitatively superior amino acids, the necessary minerals, such as calcium, phosphorus, potassium and iron, and, above all, sufficient vitamins We still need more knowledge about vitamins in diabetes, but certainly an excess of vitamins should be taken to overcome deficiencies resulting from acidosis, infections, pregnancy, etc Owing to variations in influencing factors, such as the soil and animal nutrition, variation in the values of food as purchased is great In obtaining the right diet, errors are reduced and accuracy is made possible only by weighing the food The psychic strain involved in measuring food is negligible, compared with the advantages of a measured diet

The peculiar hazards of diabetes concern the tendency to weight loss, a negative nitrogen balance and ketosis, which result from insulin deficiency and the consequent impairment of the power to oxidize and store, normally, the carbohydrate food The greater the total calories the more insulin is required or, without its use, the greater the insulin deficit Control of diabetes requires the utilization of a diet normal not only in caloric content, but in minerals and vitamins When a diet is utilized with the aid of sufficient insulin, then tissue chemistry as well as blood and urine chemistry becomes normal The respiratory quotient the glycogen content of skin liver and muscle as well as blood sugar, blood cholesterol, blood base and blood ketone content, may be returned to normal For example, young girls regain menstrual function and may become normally fertile Growth occurs with few exceptions, at a normal rate Granted that constant control at this level is difficult and almost never completely attained, the acceptance of this goal and constant striving to attain it without insulin reactions have achieved in our experience better results than have been observed in those patients who have taken insulin and maintained weight and strength, but failed to control glycosuria and blood sugar levels

Two Phases of Treatment Two phases of diabetes treatment may be used as illustrations treatment of coma and treatment of juvenile diabetes Diabetic acidosis, culminating in coma is the penalty of uncontrolled diabetes whether it is mild or severe [illegible] results when ketosis is treated as a separate entity [illegible] diabetic patient, [illegible] treatment as [illegible] of diabetes It is essentially [illegible] by

[illegible]

2 Increased metabolic needs during fever, hyperthyroidism, etc, without additional insulin
3 Pancreatic exhaustion
4 Insulin resistance produced by insulin antagonists
5 Increase in the food intake, glucose loss in the urine and ketosis from fat oxidation without insulin, in the unrecognized diabetic

We hold that ketosis in a diabetic, whether or not the patient is yet unconscious, is an emergency which becomes progressively more grave when acidosis has reached a stage measured by a reduction of the carbon dioxide content of the blood to 9 millimols per liter or less As an emergency, the patient requires constant medical attendance, preferably in a hospital where laboratory facilities are available and will be used under direction of an experienced physician at any hour of the day or night, Saturday, Sunday, or holidays Just as on an efficient surgical service we believe that no house officer or assistant resident would be expected to assume responsibility alone for the treatment of a massive gastric hemorrhage, so in diabetic coma the house staff should have the presence and advice of a staff member experienced in treatment of coma and diagnosis and treatment of the complications which are so often present Acidosis and coma are complications of diabetes, not independent entities The prime objective of treatment is to ascertain the insulin deficit and to administer the amount of insulin needed in order to secure rapid control of the diabetes and restoration of normal physiologic levels One reason for haste is that the diagnosis of the underlying complication may be impossible during severe ketosis

Our experience in the New England Deaconess Hospital with 717 patients with diabetic ketosis in whom acidosis had reached a level measured by a carbon dioxide content of venous blood of less than 20 volumes per cent or 9 millimols per liter is summarized in Table 1

We believe that the elimination of death from coma in the ninety-two patients treated between April, 1945, and May, 1948, was due to recognition of the fact that as acidosis progresses insulin resistance increases rapidly Therefore, we have tried to be more aggressive and more speedy in the administration of insulin Thus, from Table 2, it is apparent that in the earlier years only 83 units were given in the first three hours of treatment, with a mortality of 18 per cent During the years 1945–1948, 182 units were given in the first three hours, with no mortality Even these facts do not tell the entire story, because actually during the last seven years we have repeatedly recommended over the telephone that the family doctor administer large doses of insulin when the patient is at such a distance that his arrival at the hospital will be a matter of several hours In 142 patients during this time the average dose of 72 units per patient was given by the family doctors and this fact itself

undoubtedly has contributed to eliminating deaths, chiefly because it enables us to receive the patient in better condition, so that the presence of important complications can be better recognized. In five cases, between 200 and 420 units of insulin was given during the hours prior to admission. This involves an assumption of great responsibility. Obviously, if diagnosis were erroneous and a large dose of insulin was ordered over the telephone for a patient really suffering from hypoglycemia death would result. We cannot say too much about the value of the cooperation given by family doctors in reducing the incidence of death from coma.

TABLE 1

DECLINE IN MORTALITY OF 717 CASES TREATED AT NEW ENGLAND DEACONESS HOSPITAL, NINETY TWO CONSECUTIVE CASES WITHOUT A DEATH

	Cases	Mortality Per Cent
1924–1940	463	12
1940–March, 1945	162	4
April, 1945–May, 1948	92	0

TABLE 2

IMPROVEMENT IN PROGNOSIS WITH PROMPT ADMINISTRATION OF SUFFICIENT INSULIN*

	Insulin Received First Three Hours Units	Mortality Per Cent
1924–1937	83	18
1938–1944	186	11
1940–March, 1945	16	4
April, 1945–May, 1948	182	0

* [illegible] due to the [illegible] death [illegible] giving [illegible] of insulin (average per case) to 182 patients during the hours prior to their admission (1940–1948).

Treatment of Diabetic Coma. Our program of treatment of diabetic coma is summarized in the following outline.

FIRST HOUR AFTER ADMISSION

[illegible]

(b) Physical examination, noting particularly
(1) State of consciousness, type of respiration, pulse rate, blood pressure, and rectal temperature
(2) Soft eyeballs, dry tongue, dilated stomach cold and mottled skin, and impacted rectum

4 *Insulin* 100 units of crystalline insulin subcutaneously at once for adults, if blood sugar exceeds 300 mg per 100 cc and if the blood carbon dioxide content is 9 millimols per liter (20 volumes per cent) or less The dose would be proportionately less in patients with recent onset of diabetes or in young children In patients with blood sugar between 600 and 1000 mg , give 200 units additional, and with blood sugar over 1000 mg , give 300 units additional In patients in circulatory collapse, give preliminary additional doses of insulin intravenously

5 *Gastric Lavage* Use large tube, aspirate completely and wash stomach with warm water with greatest care

6 Normal saline intravenously, 2000 cc , repeated if indicated by dehydration and blood pressure below 90 mm Hg Avoid too rapid administration, especially in older patients

7 Keep patient warm yet avoid burns, as from hot water bottles

SECOND TO SIXTH HOUR

Occasionally the gravity of the case necessitates repetition of first hour's total insulin in the second hour

8 Repeat blood sugar and carbon dioxide determinations after three hours For rising blood sugar give insulin, 50–200 units, according to physician's judgment of prognosis

9 Fluids by mouth (as soon as tolerated), 100–120 cc per hour of broth, ginger ale, orange juice, tea or coffee, to be sipped by patient or spooned by nurse If nausea and vomiting recur, withhold fluids orally for 12 hours (lavage stomach again if indicated) and then resume

10 Soft or liquid food such as oatmeal gruel, orange juice or milk diluted half and half with lime water, not to exceed 10 grams of carbohydrate per hour

11 Enema for cleansing and to relieve abdominal distention

12 Record blood pressure, pulse and temperature, note signs of improvement, or the reverse

13 Urinalysis for sugar and diacetic acid every hour Record volumes

SIXTH TO TWENTY-FOURTH HOUR

14 Repeat blood sugar and carbon dioxide determinations, and give insulin 50–200 units if blood sugar and carbon dioxide levels are not improving

15 Insulin (crystalline) may now be given according to urine tests every one to four hours if fall in blood sugar has been satisfactory

If test is—	*Red*	*Orange*	*Yellow*	*Green*	*Blue*	
Give	20	16	12	0	0	Units

16 Urinary output Observe this closely and view any sign of anuria with alarm Treat with 1500 cc intravenous saline if shock is persisting Repeat as necessary For anuria, associated with hypochloremia, give 50 cc of 10 per cent salt solution intravenously Never give hypertonic

glucose solution to promote diuresis. Beware of producing excessive diuresis with consequent loss of base, especially of potassium.

SECOND DAY

17. Soft Food—Diet: carbohydrate 100 to 150 gm., protein 50 gm., fat 50 gm.
18. Protamine zinc insulin should be begun, supplemented by crystalline insulin in small to moderate doses before meals as indicated by blood sugar and urine tests.

THIRD DAY

19. Patient should gradually be returned to the standard diet for age and weight, with carbohydrate 150 to 200 gm., protein 60 to 100 gm. and fat 60 to 120 gm. daily.

Prognosis of Diabetes in Childhood.—Before the discovery of insulin, diabetic children died on an average in one to five years, usually in coma. Today the use of insulin has prolonged the average expectancy

TABLE 8

CAUSES OF DEATH ACCORDING TO DURATION OF DIABETES IN 531 DIABETICS WITH ONSET PRIOR TO 20 YEARS OF AGE

Duration Diabetes at Death Years	No. of Deaths	Coma Per Cent	Nephritis Per Cent	Heart Per Cent	Tuberculosis Per Cent	Septic Pneumonia Per Cent	Miscellaneous Per Cent
0–4.9	166	56	4	5	5	12	18
5–14.9	223	45	13	8	14	13	12
15–20+	142	5	30	37	7	9	10

to forty years according to the Metropolitan Life Insurance Company's analysis of the records of diabetic children at the George F. Baker Clinic, Boston, Massachusetts. However, after fifteen to twenty years, retinitis, albuminuria, hypertension and calcified vessels have been prevalent in persons whose diabetes dates from childhood. Table 8 shows the causes of death of 531 persons in whom diabetes had its onset between infancy and the age of 20 years. Of the 531 patients 140 died in coma, 54 of nephritis, 67 of heart disease, 29 of tuberculosis, 67 of sepsis pneumonia, and 108 of miscellaneous causes. The percentages of deaths from the various causes vary according to the duration of diabetes at the time of death, as shown in the table.

[illegible] results are [illegible] for diabetics [illegible]. It is to be noted that after fifteen years of diabetes [illegible] patients have gangrene, sclerotic nephritis and cardiovascular disease, [illegible] [illegible] in the patients [illegible] Thus White [illegible] [illegible] 1923 [illegible] with diabetes

betes of twenty years duration, 75 per cent of the 50 patients with severe damage by arteriosclerosis had coma Of 114 patients with less severe damage, only 40 per cent had had coma, and of twenty-eight patients in whom no arteriosclerosis was found, only 15 per cent had had coma It is the lack of diabetic control which favors early arteriosclerosis Twenty-eight of these 192 patients have survived 20 to 25 years of diabetes and are still free from calcified arteries, albuminuria, hypertension and retinitis

Let us cite the reports of two such patients

CASE IV (19347) —Diabetes had developed in this boy in 1924, at the age of 9 years and 10 months Insulin was started and has been continued ever since The patient has never had coma On the contrary, he has attempted to keep the urine sugar free and has made his own tests frequently He came for a check-up in December, 1947, because he wished to marry Blood pressure was 130/90, and the urine was free from albumin and sugar Blood sugar values were 139 and 103 mg per 100 cc on a diet of 165 gm of carbohydrate, 80 gm protein, and 100 gm fat, with 10 units of crystalline zinc insulin and 50 units of protamine zinc insulin X-ray examination showed no calcification in aorta, pelvic vessels or leg arteries No retinal hemorrhages were found, and capillary fragility tests were normal

CASE V (5301) —Diabetes developed in this girl in 1916, when she was 12 years old Insulin was begun in 1923 when she was in college In June, 1926, when she was first seen in the New England Deaconess Hospital, the urine contained 0 2 per cent sugar and blood sugar ranged from 140 to 260 mg per 100 cc In January, 1948, she returned for a check-up, her last examination having been in March, 1941 She now takes regular insulin four times a day, beginning at 3 30 A M , and by making her own tests for acetone and glucose avoids glycosuria and acetonuria As in case IV, there were no retinal hemorrhages or exudate, and x-ray examination revealed no calcification in leg arteries or aorta and only a trace in pelvic vessels Not only is the patient actively and cheerfully at work as a chemist in western Massachusetts, but she contributes to the support of a boy whom she has never seen, who is studying chemistry and working his way through a mid-western university "The will to live begets the will to give" is a motto which has already been put in practice by other diabetics

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CURRENT METHODS OF TREATING THYROTOXICOSIS

WILLIAM H BEIERWALTES, M D* AND CYRUS C STURGIS M D, F A C P†

TODAY the physician is less certain which therapeutic plan to employ in the treatment of thyrotoxicosis than he was ten years ago Then the standard treatment used in a great majority of such patients was the administration of iodine for ten to fourteen days, followed by a subtotal thyroidectomy The most important therapeutic innovation has been the introduction of new antithyroid agents, such as thiouracil and propylthiouracil Their use has raised the following questions First, is the therapeutic effect of these newer drugs equal or superior to the results following subtotal thyroidectomy? And second, is it possible to prepare the patient for surgery more effectively by the use of propylthiouracil or allied compounds in combination with iodine? The primary purpose of this discussion is to offer some suggestions which have a practical bearing on these two questions Reference also will be made briefly to the therapeutic use of radioactive iodine, which has great possibilities as an agent to control the manifestations of toxic goiter The present experience with this form of treatment is too limited, however, to express a definite opinion concerning it

THYROID PHYSIOLOGY IN RELATION TO THERAPY

A basic knowledge of the physiology of the thyroid gland, and of the changes which result from the various forms of therapy for thyrotoxicosis, is essential for a clear understanding of the management of patients with such a condition

Pituitary-Thyroid Axis —One of the important concepts of thyroid gland physiology is its hormonal relationship to the anterior lobe of the pituitary gland Figure 150 shows this relationship diagrammatically The arrow from the pituitary to the thyroid gland indicates the stimulating action of the thyroid stimulating hormone known as T S H The anterior lobe of the pituitary gland thus stimulates the thyroid gland to secrete thyroxine its circulating hormone The arrow from the thyroid gland to the pituitary gland indicates in turn the inhibiting action of thyroxine on the output of T S H of the anterior pituitary Thus a

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regulatory system is established whereby each gland tends to control the hormonal output of the other

If, for example, the output of thyroxine is decreased, due to primary disease of the thyroid, or following the administration of an antithyroid drug, then the inhibiting action of thyroxine on T S H by the pituitary gland is diminished and hence an *increased output of T S H will occur* This latter action will be referred to throughout the remainder of this paper and must be constantly kept in mind when treating patients with thyrotoxicosis

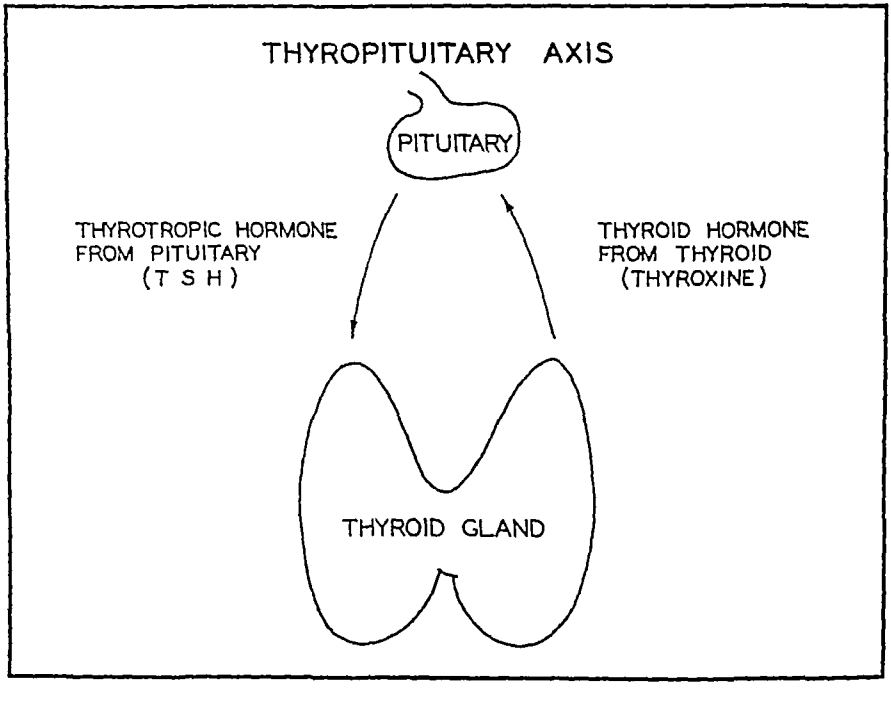


Fig 150 —Thyroid-stimulating hormone (T S H —left) from anterior pituitary stimulates output of thyroid hormone (thyroxine (?), right) which in turn decreases output of T S H from anterior pituitary, thus maintaining an endocrine balance between these two glands

The Formation of Thyroxine.—Figure 151 diagrammatically represents the biochemical steps in the formation of thyroxine At the left, iodides are represented as entering the gland These are derived from the diet and from the breakdown products of organic iodides in the body This iodide accumulates in the follicular cells where it is acted upon by the peroxidase enzyme system[1] in the presence of manganese and oxygen, to liberate free iodine The latter combines immediately with the amino acid, tyrosine, to form diiodotyrosine, as shown by the chemical formulas below Two molecules of diiodotyrosine are then united, again

in the presence of a cytochrome, in an oxygen linkage to produce thyroxine. Thyroglobulin, the substance identified within the follicles by the microscope as "colloid," is the storage form of thyroxine and is a protein substance made up of diiodotyrosine and thyroxine in a peptide linkage.[2]

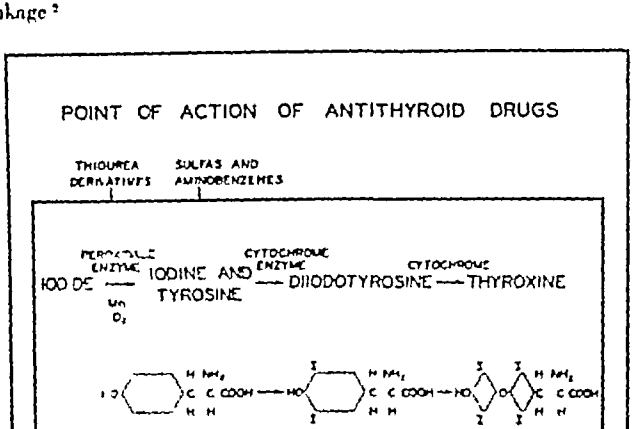


Fig. 151. Free iodine is liberated from iodide in the presence of peroxidase enzymes and oxygen. Iodine combines immediately with tyrosine in the presence of cytochrome to form diiodotyrosine. Two molecules of diiodotyrosine are then joined in an oxygen linkage (ether) to form thyroxine. Formulas for these amino acids are given below. Point of action of antithyroid drugs are indicated above.

ACTION OF ANTITHYROID DRUGS

Propylthiouracil. Reference to Figure 151 will show that the thiourea derivatives (thiouracil, propylthiouracil, etc.) produce a therapeutic effect by depressing the peroxidase enzyme system. By so doing a specific action, they decrease the rate of release of free iodine from iodide. Hence, as less free iodine is available for combination with tyrosine, the rate of formation of thyroxine is greatly retarded. The thyroxine present in the gland [illegible] to the administration of the propylthiouracil and other antithyroid drugs is [illegible] the blood stream and metabolized. [illegible] the thyroid gland [illegible] to [illegible] the [illegible] the [illegible] rate. The less [illegible] of thyroxine is necessarily dependent upon [illegible]

thyroid state is relieved The decreased blood thyroxine level, however, removes the inhibiting action on the production of T S H by the anterior pituitary gland and an increased amount of this hormone is produced As a result of this there is increased hyperplasia, hypertrophy, and vascularity of the thyroid gland These anatomical changes appear paradoxical in the presence of the clinical subsidence of thyrotoxicosis due to the enzyme block within the thyroid gland produced by propylthiouracil

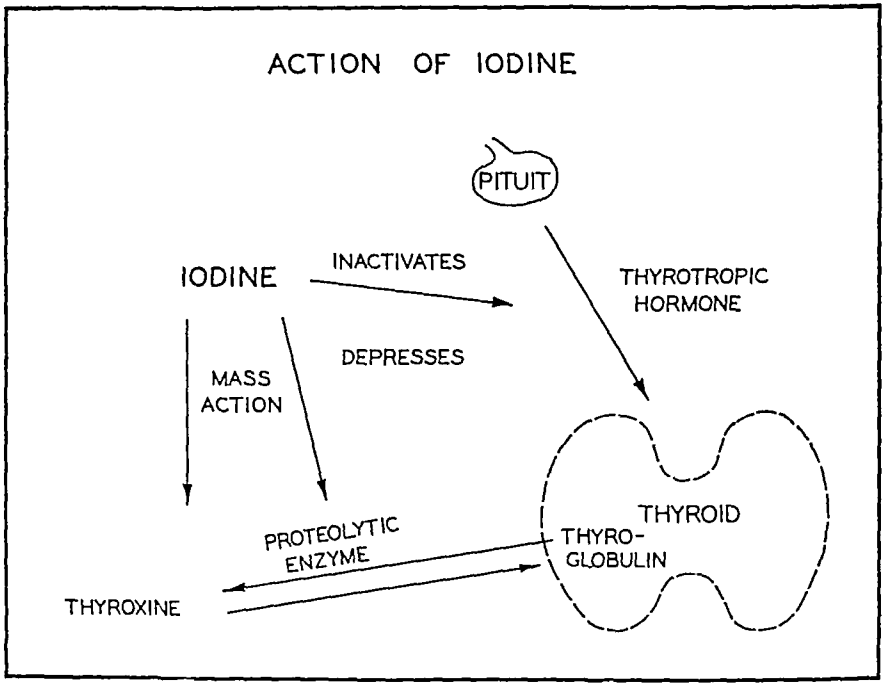


Fig 152 —The three principal actions of antithyroid drugs are diagramed here as (1) inactivation of thyrotropic hormone, (2) depression of the rate of proteolytic enzyme activity, and (3) adding one of the products of a reversible chemical reaction, thus tending to force the reaction in the direction of storage.

Aminobenzenes and Aniline Dye Derivatives —The aminobenzenes of which para-aminobenzoic acid is most well known, and the sulfonamide drugs such as sulfadiazine, are thought to act at the second point[1] shown in Figure 151 by competing with tyrosine for combination with free iodine This serves to block the chemical production of thyroxine and exactly the same chain of events ensues as described above

Iodine —Although iodine has been used for many years as an antithyroid agent its mechanism of action has not been clarified until recent years Figure 152 presents the three principal actions of this drug

The first action shown at the top right of the figure, inactivation of

the T S H is thought to occur at the level of the thyroid cells and decreases the amount of available T S H to stimulate thyroid tissue. With the decrease in this stimulus, the thyroid gland tends to revert to a resting state with the morphology of an iodinated thyroid. This action, plus the fact that thiouracil and iodine exert their effects in depressing thyroxine production at different points, makes it understandable why the simultaneous administration of the two agents causes a more rapid reduction in the basal metabolism rate than when one alone is given.[5] This is a great advantage to both the surgeon and the patient because

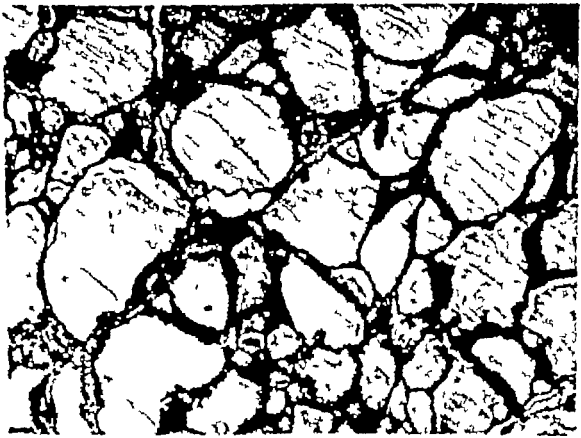


FIG. 133. Microphotograph of surgical pathological specimen of the thyroid after the patient was treated for [illegible] with saturated iodide water with [illegible] per day for surgery with [illegible] (preoperative [illegible]) [illegible] of Lugol's solution per day given simultaneously until the day of operation. (Courtesy of Dr. [illegible] Weller, Department of Pathology, Temple University Medical School.)

[illegible] longer is it considered necessary to discontinue thiouracil on the day of metabolism has reached normal and then a minimum interval of three weeks to permit the gland for surgery. Evidence that iodine when given simultaneously with thiouracil is adequate preparation of the gland for surgery is shown by the microphotograph of the thyroid of a patient with exophthalmic goiter prepared in this manner (Fig. 133).

Iodine also has a special [illegible] which reduces the basal metabolic rate. It [illegible] the rate of metabolism and the [illegible] of the [illegible] effect [illegible] the larger [illegible] than

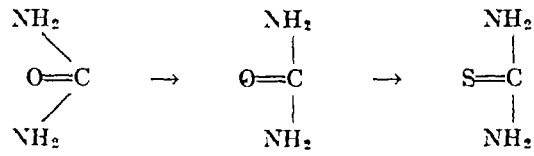
globulin with a molecular weight of 700,000, into the small molecule thyroxine, with a molecular weight of 69,000[6] so that it can be released into the blood stream This depression of proteolytic enzyme function by iodine is accomplished both by inactivation of T S H , which normally controls the rate of activity of the proteolytic enzyme, and by actual chemical combination with the enzyme When the rate of release of thyroxine is decreased, of course the metabolic rate falls

Salter has demonstrated in vitro a third possible antithyroid action of iodine As stated, a proteolytic enzyme normally aids the breakdown of thyroglobulin to thyroxine and other substances When one adds iodine to the solution in vitro, however, it tends to force the reaction in the opposite direction, i e , formation of thyroglobulin rather than thyroxine, by virtue of the simple law of mass action [7]

EFFECTIVENESS OF SPECIFIC ANTITHYROID AGENTS, PARTICULARLY PROPYLTHIOURACIL

Propylthiouracil is at present the most commonly used medical antithyroid agent and once its indications and contraindications are understood, the use of other forms of treatment is simplified

Thiourea is formed from urea as follows



The oxygen atom attached to carbon is replaced by a sulfur atom (s) to form the carbon-sulfur or "thio" group Figure 154 shows the chemical derivation of propylthiouracil from thiourea Dotted lines encircle the thiocarbamide group on the left, which is considered essential for activity, and the sixth carbon atom of the nucleus that is the site of substitutions affecting further the activity of thiouracil derivatives [8]

Table 1 shows the first ten of these newer drugs as listed by Williams[9] in order of decreasing effectiveness

Toxicity.—In general, the more active of these drugs were found to be the least toxic For some time propylthiouracil was thought to be without untoward effects While no fatalities have been reported as due to this drug, it must be kept in mind that three cases of agranulocytosis and eleven instances of severe leukopenia have been reported [10] Agranulocytosis and drug fever are the only toxic reactions that will require dis-

continuing this drug.[11] Although these complications of treatment occur rarely, the physician should warn the patient that if fever, sore throat, skin rash, lymphadenopathy or malaise develops, the drug should be omitted immediately and a white and differential blood cell count done at once. If a leukopenia of less than 4000 white blood cells per cubic millimeter, or a polymorphonuclear percentage of 30 per cent or less is present, the drug should be discontinued and penicillin administered to prevent or control sepsis. Since leukopenia is commonly observed in an

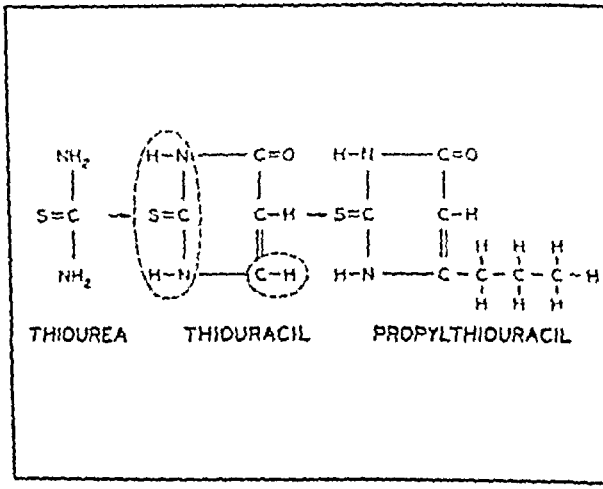


Fig. 150 - Detoxication of propylthiouracil from the urine. Model [illegible]

[illegible] therapy is instituted [illegible] as a reference [illegible] These rules have been [illegible] in a recent article by the author [illegible]

Arthritis [illegible]

no significant difference in response from our first seventy-four patients treated with 0 6 gm of thiouracil a day Since 0 6 gm of thiouracil was judged to give the optimum response, then propylthiouracil would appear to be four times as effective as thiouracil in patients It has been our clinical opinion, however, that many patients respond more rapidly to 300 mg than to 150 mg daily of propylthiouracil, and the former (100 mg three times daily, before meals) is the dose we recommend for routine use until the basal metabolic rate reaches zero

TABLE 1

ANTITHYROID DRUGS IN ORDER OF DECREASING EFFECTIVENESS, WITH THREE CHEMICAL FORMULAS

1 6 Propylthiouracil

and 6-Cyclopropylthiouracil

2 6-Isobutylthiouracil

3 6-Butylthiouracil

4 6-Methylthiouracil

5 Thiouracil

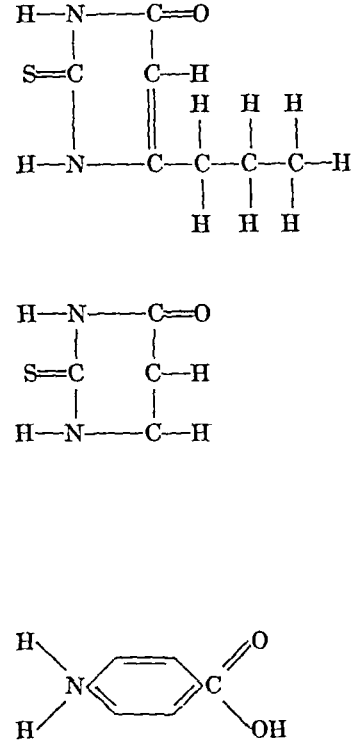
6 Ortho-Phenylenethiourea

7 Tetramethylthiourea

8 Thiothymine

9 Aminothiazole

10 Para-Aminobenzoic Acid



(After Williams)

Figure 156 shows a more satisfactory response in the twenty-two patients we have treated with 300 mg daily as compared to forty-two patients who received 150 mg The superior response, however, cannot be attributed entirely to the greater dosage since 4 minims of Lugol's solution per day was given simultaneously with the propylthiouracil Also these patients had treatment started without benefit of a control period of bed rest due to the severity of the disease Four patients treated with only 150 mg of propylthiouracil per day, but with added

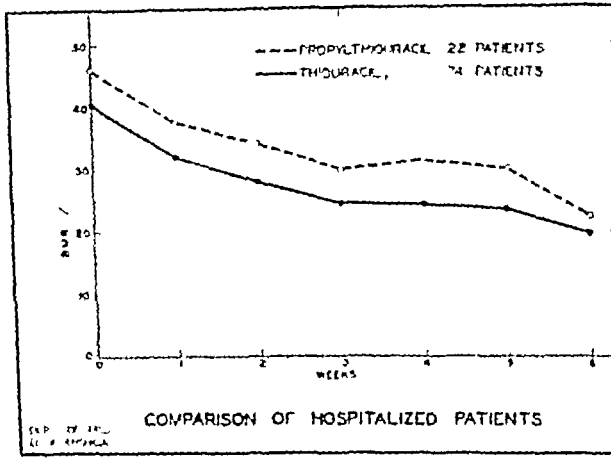
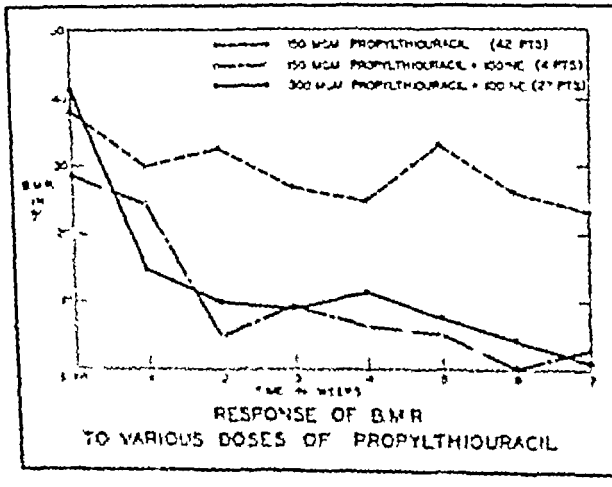


Fig. 1.5 – Comparable response of twenty two patients treated with 150 mg. of propyl thiouracil a day and seventy four patients treated with 600 mg. of thiouracil a day indicates that the former drug is four times more effective than the latter, by weight. (J. Lab. & Clin. Med.)



iodine, enjoyed as rapid a response as twenty-two patients who received 300 mg daily, although there are too few patients to be statistically significant Further studies may cause us to conclude that a daily dose of 150 mg of propylthiouracil plus 4 minims of iodine is satisfactory for routine use

STATUS OF SURGICAL AND MEDICAL TREATMENT WITH PROPYLTHIOURACIL

Should propylthiouracil therapy alone be used as a substitute for subtotal thyroidectomy with preoperative iodine therapy? To answer this question the following points should be considered First, what percentage of patients presenting themselves to the physician will be cured with propylthiouracil and iodine as the sole form of therapy, second, how long will the cure take, and third, what is the morbidity of

TABLE 2

PRESENT STATUS OF 200 PATIENTS TREATED WITH THIOURACIL AND PROPYLTHIOURACIL

Dead	10
Thyroidectomy	60
Still on propylthiouracil	70
Drug discontinued	
Relapse	10
No relapse	34
Lost from follow-up	16
Total	200

the treatment In an attempt to answer these questions, an analysis was made of the results in the first 200 of our patients treated with thiouracil and propylthiouracil, two months or longer, between April 1944 and June 1947, and followed through November 1947

Table 2 shows the status of these 200 patients at present Sixty of these patients had a thyroidectomy after an average preparation of 3 9 months Surgery was employed because of a huge goiter, substernal goiter, pressure symptoms, nodular goiter, febrile or agranulocytic reactions to the drug, and slowness of response Ten patients died of unrelated causes including suicide, myocardial infarction and cerebrovascular accident Forty-four have stopped their antithyroid drug Seventy are still under treatment and remain potential candidates for a "medical cure" after an average period of nine months Sixteen have been lost from our follow-up because of change of residence, transference of their care to another physician, or unreliability in taking treatment or reporting for follow-up

Ten patients, or 23 per cent of the group that discontinued propylthiouracil, suffered a relapse Table 3 summarizes the important fea-

tures of this group. Some stopped the drug of their own volition and some at our request in an effort to *produce cure*.

Table 4 shows the same features averaged in the group of thirty-four patients, or 77 per cent, who have experienced *no recurrence of thyrotoxicosis* to date after stopping propylthiouracil.

The significant points to be gained from a comparison of the group in whom the thyrotoxicosis was adequately controlled and those in whom relapse occurred, are arranged *for direct* comparison in Table 5. The "curable" patients are seen to have, usually, a non-nodular goiter, to be relatively young, to have been treated for about eleven months,

TABLE 5

RELAPSE IN TEN PATIENTS AFTER DISCONTINUING THIOURACIL

Name	Hosp. Number	Sex and Age	Goiter Size*	Initial B.M.R.	Duration of Treatment Before Discontinuing	Duration of Normal B.M.R. Before Disc.	Duration of Remission Before Recurrence
D. A.	[illegible]	M 53	–	+23	3	3	1
J. C.	[illegible]	F 16	+	+31	8	4	2
R. C.	[illegible]	M 59	+ N	+39	10	12	2
C. S.	[illegible]	M 53	+	+20	13	1	2
				+30	5	1	3
L. L.	[illegible]	F 49	+ + + N	+33	1	0	0
J. T.	[illegible]	F 5[illegible]	+ +	+32	4	2	2
A. G.	[illegible]	F 7[illegible]	+ N	+19	11	6	1
L. H.	[illegible]	M 6[illegible]	+ + + N	+23	3	1	–
R. L.	[illegible]	F 41	+ N	+19	8	7	4
[illegible]	[illegible]	F 30	+ +	+39	2	1	1
Average		[illegible]		[illegible]	[illegible] mos.	[illegible] mos.	[illegible] mos.

* [illegible] to [illegible] "N" after goiter size [illegible] that the goiter was [illegible]

and to have enjoyed a normal metabolism for seven months or more before the drug was stopped. To recapitulate, the sustained improvement was produced chiefly in the non-nodular goiter group. Ninety per cent of the relapses occurred in the nodular goiters. The cured patients were in the average fifteen years younger. They were treated two [illegible] longer before discontinuing the drug. The basal metabolic rate was within normal limits three months. The longer but to the drug was [illegible] and the average treatment fourteen months. The longer as it has proved to be a factor. It is important to note that 80 per cent of the patients who responded well to the drug after treatment was [illegible] This was [illegible] the [illegible] also made by us in 1948

TABLE 4

NO RELAPSE IN THIRTY-FOUR PATIENTS AFTER DISCONTINUING PROPYLTHIOURACIL

Name	Hosp Number	Sex and Age	Goiter Size*	Initial B M R	Duration of Treatment Before Discontinuing	Duration of Normal B M R Before Disc	Duration of Remission (through Nov 1947)
A B	593356	F 19	++	+46	14	12	3
G B	583541	F 31	+++	+18	5	2	18
J C	495571	M 43	0	+21	8	5	36
C D	St Jos	M 32	++	+28	14	12	27
V D	547212	F 24	++	+19	24	21	13
E H	562677	F 40	++	+27	7	6	27
W J	549057	M 24	+	+23	5	4	33
S K	551224	F 48	+	+35	16	14	12
H L	356822	F 32	+	+15	4	2	9
J L	550744	F 26	0	+39	13	10	24
J L	553620	F 27	++	+19	9	8	19
D M	586004	M	+ N	+38	5	1 5	8
D P	564624	F 26	++	+28	5	4	30
A P	576177	F 43	++		7		12
L P	596163	F 35	+++	+35	12	5	4
J S	573015	M 27	+++	+56	21	17	8
J S	586008	F 58	++++	+48	15	1	4
A S	585487	M 60	0	+23	9	5	7
E T	558024	F 45	+	+27	13	12	20
M V	171309	F 70	+++ N	+37	8	3	20
J V	436302	M 46	0	+47	4	2	5
J W	566623	M 54	+	+28	8	6	23
F W	P R	F 44	0	+20	2	1 5	36
D W	602021	F 69	0	+33	9	5	4
L W	191131	F 67	++ N	+30	13	1	3
A R	463451	F 17	+++	+35	12	6	29
Z R	564594	F 64	++	+41	24	23	8
M P	537829	F 27	++	+24	14	10	20
R G	550664	F 21	++	+31	12	11	30
D R	564374	M 17	++	+60	12	2 5	21
D S	559978	F 17	+++	+65	8	4	30
D S	395252	F 14	++	+39	14	4	6
T S	590214	F 66	+++ N	+32	9	—	10
M S	566056	F 15	+++	+56	18	14	17
Average		*35 yrs*		*34%*	*10 6 mos*	*7 3 mos*	*17 mos*

* See footnote to Table 3

and confirmed by Williams[14] that if a remission persists more than four months following cessation of therapy, the patient will usually continue in that state for an undetermined but relatively long interval Although

many of our patients have now been in good health for from two to three years after discontinuing thiouracil, the relapsing tendency of thyrotoxicosis following any form of treatment must be kept in mind when the word "cure" is used!!

TABLE 5

Results in Patients Who Discontinued Propylthiouracil

	Average Age	Per Cent Nodular	Average Initial B M R	Average Duration of Treatment Before Discontinuing, Months	Average Duration of Normal B M R Before Discontinuing, Months	Average Duration of Remission, Months
Relapse 10 patients	48	50	40%	8.4	4	2.8
No relapse 34 patients	35	11.7	31%	10.6	7.3	17

TABLE 6

Results of Subtotal Thyroidectomy in 150 Cases of Graves' Disease (Diffuse Toxic Goiter) 1933–1940

	Per Cent
Satisfactory results	
Return to good health	61.3
Hypothyroidism	12.9
Exophthalmos	7.7
Unilateral temporary vocal cord paralysis	2.3
Bilateral temporary	1.5
Total	85.6
Unsatisfactory results	
Recurrent thyrotoxicosis	8.5
Bilateral paralysis	0.8
Unilateral paralysis	0.8
Death	3.3
Total	14.4

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It is clear that these results compare favorably with those of surgery. Table 6 shows the comparative morbidity and mortality analysis of a large group of cases treated by subtotal thyroidectomy. In this particular series of 150 cases 85 per cent were cured. Surgery therefore is superior

to propylthiouracil in achieving a higher percentage of cures and accomplishing this in a shorter interval Propylthiouracil therapy, however, has no mortality, no permanent hypothyroidism, parathyroprivia, or laryngeal palsy The relative merits of propylthiouracil therapy on the one hand and surgery on the other, might be summarized then by saying that (1) surgery cures a higher percentage of patients with thyrotoxicosis, (2) in a shorter period of time (3) but with a greater risk to the patient, (4) always with the expense of hospitalization, and (5) it interferes with the patient's work for a considerable period of time

From the standpoint of the highest percentage of cures in the shortest possible period of time, probably the treatment of choice in the average patient is still the use of Lugol's solution, with the patient in a hospital under sedation, followed by subtotal thyroidectomy Our main point, however, in treating the thyrotoxic patient in the first place is to (1) avoid disability and (2) to prevent death The operative mortality in the surgical clinics which have had a special interest in thyroid surgery has dropped from 3 per cent to 0 1 per cent[10] since thiouracil and propylthiouracil have been used preoperatively On this basis, therefore, any patient with more than a minimally elevated basal metabolic rate and other complications that might increase the operative morbidity should have propylthiouracil as preoperative medication

The patients with lesser degrees of thyrotoxicosis, or with small exophthalmic goiters, have a 75 to 80 per cent chance (as in surgery) of obtaining a satisfactory cure on propylthiouracil alone in an average period of one year without the necessity of discontinuing work during treatment, or being exposed to significant operative morbidity

Nodular Goiters —Toxic nodular goiters, if large, should always be treated surgically because of the incidence of degenerative and malignant change which they undergo, the presence of pressure symptoms, the presence of toxicity per se, and in some instances for cosmetic reasons alone

A full discussion of malignancy of the thyroid gland will not be presented here, as the main topic under consideration is the treatment of thyrotoxicosis It should be pointed out, however, that malignant disease rarely, if ever, arises in a normal gland, with the possible exception of lymphosarcoma Furthermore, in our experience it is exceedingly uncommon for a cancer to arise in a thyroid gland with a solitary nontoxic adenomatous nodule, but it does occur in those with multiple nodular goiters, and also in patients with toxic adenomas In fact, we do not consider that toxicity in a nodular goiter in Michigan is a guarantee against cancer of the thyroid gland since 26 per cent of all the proven carcinomas of the thyroid gland at the University of Michigan Hospital were removed from patients who had evidence of thyrotoxicosis [15] In

other words, when all of the patients with carcinoma of the thyroid gland were considered, about one in four had thyrotoxicosis

SUMMARY OF INDICATIONS FOR THE USE OF PROPYLTHIOURACIL

1 The drug should be employed as preoperative treatment in all cases of toxic goiter except possibly those with minimal toxic symptoms In such cases, perhaps the use of iodine alone is permissible with the operation performed after a two week period of preparation In our opinion however, because a patient with mild toxic goiter occasionally has a severe postoperative course, and because, the patient treated with propylthiouracil is delivered to the surgeon in a much better condition than following iodine therapy alone it seems preferable to prepare all patients for subtotal thyroidectomy with propylthiouracil and iodine

2 It is permissible to use propylthiouracil and iodine as the sole form of therapy in an attempt to cure the following patients those with persistent or recurrent thyrotoxicosis following thyroidectomy, patients over 50 years of age with severe heart disease, those patients who are considered to be too old to withstand operative procedures, patients with vocal cord paralysis or parathyroid tetany those who refuse subtotal thyroidectomy and finally, patients with exophthalmic goiter in whom the gland is inconspicuous and in whom there are no pressure symptoms

The Use of Propylthiouracil in Patients with Toxic Adenoma. In our opinion this drug in combination with iodine should be employed in the treatment of toxic adenoma *only as a preoperative measure* All such patients should have a subtotal thyroidectomy after such preoperative treatment, provided their general condition is such that they will withstand a major operative procedure Those who will not survive such an operation after adequate preparation are few in number

SPECIFIC DETAILS OF THERAPY WITH PROPYLTHIOURACIL

In our experience the most efficient method of preparing patients is to administer 100 mg of propylthiouracil three times daily before meals supplemented with 4 drops of Lugol's solution daily The therapeutic regimen should be maintained until the basal metabolic rate is zero and the thyrotoxicosis is adequately controlled, as judged by the subjective symptoms Then a subtotal thyroidectomy should then be performed with as sharp as the operation No specific antibiotic treatment is required for preoperative [illegible]

[illegible]

metabolic rate when the patient is receiving this dosage suggests that the medication may be discontinued with a strong possibility that the remission will continue for a long interval In general, it is advisable to continue the medication until the basal metabolic rate has been maintained below zero for ten months When this is done, the expectation of a "cure' is about 80 per cent Progression of exophthalmos during therapy is an indication for the simultaneous administration of 0 065 gm of desiccated thyroid a day to depress the output of thyrotropic hormone

From the previous discussion, therefore, it is apparent that we consider surgery to be the mainstay of treatment in thyrotoxicosis Propylthiouracil is of great value, however, as preoperative treatment to lower surgical mortality and morbidity, and in patients in whom the morbidity of surgery does not justify surgical treatment of the thyrotoxicosis present This evaluation of the place of surgery and propylthiouracil therapy greatly simplifies the discussion of the remaining antithyroid agents, namely, radioactive iodine, roentgen ray therapy and iodine

INDICATIONS FOR THE USE OF OTHER ANTITHYROID AGENTS

Radioactive Iodine.—In recent experiments on the thyroid gland of animals[16] the pathologic effects of beta radiation from radioactive iodine, I^{131}, have been noted Doses of 300 millicuries of I^{131} were injected subcutaneously into rabbits and dogs Pathologic examination of the thyroid glands in these animals revealed that by the tenth day there was extensive necrosis, hemorrhage, polymorphonuclear infiltration, and changes in all the layers of the thyroid arteries A dog sacrificed 100 days after the injection showed almost complete destruction of the thyroid gland and partial or complete occlusion of the arteries and veins In one rabbit there was damage to the renal tubules Four millicuries per pound of body weight to rabbits produced complete destruction of the thyroid gland and some injury to the trachea and the renal tubules These observations indicate that this radioactive element has a profound destructive effect on the thyroid gland They also show that these effects are not limited to the thyroid gland when large quantities of radioactive iodine are used

The indications for the use of radioactive iodine in thyrotoxicosis are the same as those for propylthiouracil, and for the same reasons In our opinion, however, its use is limited by the expensive equipment necessary to control its application properly Furthermore, the possible long-term complications such as irradiation nephrosis, parathyroprivia, irradiation of fetus and ovaries, pulmonary fibrosis or carcinoma have not been adequately evaluated We have limited its use, therefore, to patients who cannot be treated by surgery or propylthiouracil In treating cancer of the thyroid gland, especially when metastases are present,

radioactive iodine may be of great value. In our experience, however not all metastatic lesions will take up iodine, and hence the administration of this therapeutic agent in such cases would be useless. In others, however, the radioactive material is picked up by the metastatic lesions, as determined by the Geiger counter, and hence subjects them to intensive effective irradiation.

Roentgen Ray. — The use of the roentgen ray in the treatment of toxic thyroid conditions is no longer recommended, although in the past encouraging results have been attained in some patients. The limiting factor has been the inability to apply a satisfactory dose to the thyroid parenchyma because of the sensitivity of the overlying skin and the underlying trachea. This factor is eliminated when radioactive iodine is given.

Iodine. — This element is valuable in causing involution of the thyroid to the colloid state and accelerating the response of the patient to propylthiouracil. It should be employed alone as preoperative therapy rarely and then only in the patients with mild exophthalmic goiter. Otherwise it has been supplanted by the combination of iodine with propylthiouracil. The response of toxic nodular goiters to iodine alone is poor as compared to the response of the so-called "exophthalmic goiter." The therapeutic effect produced in toxic nodular goiter with iodine and propylthiouracil is satisfactory.

SUMMARY

1. A basic knowledge of the physiology of the thyroid gland and the alteration of its normal function by antithyroid agents is necessary, in order to treat patients intelligently under varied conditions.

2. The administration of iodine followed by subtotal thyroidectomy may be employed in patients with uncomplicated exophthalmic goiter who have only mild toxicity. A more satisfactory result is attained by the use of propylthiouracil plus iodine. This group also has the highest incidence of cure with propylthiouracil and iodine alone.

3. The optimum preoperative treatment of patients with toxic nodular or [illegible] goiter of moderate to severe toxicity is 200 mg. of propylthiouracil and 4 drops of Lugol's solution per day. Digitalis and [illegible] contraindicated. Iodine should be taken at least zero.

4. All [illegible] exophthalmic goiters and all nodular toxic goiters should be [illegible]

[illegible] propylthiouracil with iodine may be most advantageous as an attempt to [illegible] patients at [illegible] with high [illegible] [illegible] of recurrence in a selected group [illegible] [illegible] of the [illegible] iodine are those of [illegible] [illegible] as possible danger to patient and

metabolic rate when the patient is receiving this dosage suggests that the medication may be discontinued with a strong possibility that the remission will continue for a long interval In general, it is advisable to continue the medication until the basal metabolic rate has been maintained below zero for ten months When this is done, the expectation of a "cure" is about 80 per cent Progression of exophthalmos during therapy is an indication for the simultaneous administration of 0 065 gm of desiccated thyroid a day to depress the output of thyrotropic hormone

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SUMMARY

1 A basic knowledge of the physiology of the thyroid gland and the alteration of its normal function by antithyroid agents is necessary, in order to treat patients intelligently under varied conditions

2 The administration of iodine followed by subtotal thyroidectomy may be employed in patients with uncomplicated exophthalmic goiter who have only mild toxicity A more satisfactory result is attained by the use of propylthiouracil plus iodine This group also has the highest incidence of "cure" with propylthiouracil and iodine alone

3 The optimum preoperative treatment of patients with both nodular and non nodular goiters of moderate to severe toxicity, is 300 mg of propylthiouracil and 4 drops of Lugol's solution per day This should be continued until the basal metabolic rate is at least zero

4 All large exophthalmic goiters and all nodular toxic goiters should be removed surgically

5 Propylthiouracil with iodine may be used alone in an attempt to produce a "cure" in the remaining patients, and in cases with high surgical mortality, with an 80 per cent chance of success in a selected group

6 The indications for the use of radioactive iodine are those of propylthiouracil with other limitations such as possible danger to patient and

the difficulties of securing the material and controlling its use Further experience with this form of therapy, under carefully controlled conditions, is necessary before it can be recommended for widespread use

7 The chief use of iodine today in treating patients with thyrotoxicosis is in augmenting the antithyroid effect of propylthiouracil and in reducing the hyperplastic changes produced with propylthiouracil preoperatively

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ELECTROSHOCK THERAPY FOR DEPRESSION

Report of 200 Cases

NATHAN SAVITSKY, M D * AND WILLIAM KARLINER, M D †

IN 1938 Low[14] and his co-workers noted that manic-depressive episodes responded favorably to metrazol convulsive therapy, originally suggested by Meduna[16] in 1935 for schizophrenia Shortly afterward, Bennett[3] reported encouraging results with convulsive therapy in depressions

In 1938 Cerletti and Bini[6] introduced electrical induction of convulsions as a substitute for metrazol, and the method soon almost completely displaced metrazol in the treatment of affective disorders Electroshock therapy requires less time and is easier to administer It produces a less intense seizure, with fewer skeletal complications There is always complete amnesia for the treatment with electroshock In this way the psychic trauma of intravenous injections is avoided, for with metrazol the patient usually does not have complete amnesia for the period before loss of consciousness Electroshock therapy therefore has become the preferred method in the treatment of affective disorders

Hematoporphyrin,[10] glycine,[29] synhexyl[26] and lactic acid[18] have all been used in depressions without success Estrogenic substances for involutional depressions have proved equally inefficacious We can confirm the experience of Bennett and Wilbur[4] who conclude, after studying 500 women with depressions during the menopausal period, that estrogenic hormones have no place in the treatment of these patients except for symptomatic relief of vasomotor symptoms Benzedrine and dexedrine sulfate are of some value in very mild depressions The favorable response of all types of depressed patients to electroshock therapy leaves no doubt as to its superiority

In view of the definite tendency to spontaneous remissions, it is advisable to watch every depressed patient for a week or two before beginning treatment Spontaneous improvement is sometimes noted before treatments are begun We repeatedly observed patients who appeared extremely depressed at the time of the first examination but who were perfectly well a week or two later when they came for re-examination or for their first treatment These patients were not treated but were kept under observation Patients who were very agitated and suicidal and

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who refused food were treated soon after their initial interview because of the risk of self-destruction or of severe malnutrition The danger of suicide even in milder depressions cannot be overemphasized All depressed patients are potentially self-destructive Strict supervision is important during the period of observation before treatment is begun Suicidal attempts were made by a few patients while awaiting treatment The justification for the widespread use of electroshock therapy, despite its dangers and complications, is that depressive states are serious ailments The incidence of suicides in our experience has been strikingly reduced, compared with their frequency before the introduction of shock therapy All patients with depressions, including the neurotic and reactive variants, are suicidal Attempts at suicide are not infrequent during the period of recovery, perhaps because of the absence of severe retardation The risk of suicide is usually greater during the early morning hours One attempt is often followed by others Patients occasionally deny suicidal thoughts or inclinations in order to avoid any interference with their plans for self-destruction

Depressions are common affections They are frequently not recognized as such, sometimes masking as physical ailments when gastrointestinal and other so-called organic complaints dominate the picture The patients may not complain of depression at all When dejection is noted by the clinician, it is often interpreted as a normal reaction to persistent ailing We can corroborate the observation of Adamson[1] that the treatment of the physical complaint does not usually help the depression If treatment is continued long enough, spontaneous remission of the depression sometimes sets in On rare occasions so-called neurotic equivalents of depressions increase the difficulty of recognition of the underlying psychosis We have encountered, as Stengel[25] did, manic-depressive patients who had otherwise inexplicable attacks of uncontrollable vomiting for a few weeks We have also observed diarrhea, severe headache, intense epigastric distress, inordinate dryness of mouth and distressing dyspnea as equivalents of manic-depressive psychosis It is important to look for depression in patients of this type

Differentiation between the psychoneuroses and endogenous depressions is important Endogenous depressions often show marked diurnal variation, the dejection usually being worse in the early morning, with frequent marked inability to "get started " Some patients may appear almost normal toward evening and may even plan for the next day but then find themselves unable to do anything the following morning Such diurnal variation is not often encountered in neurotics The psychoneurotic usually reports feeling better when occupied, welcoming work as a means of temporary relief The depressed patient is often utterly unable to work and there is in almost all cases a slowing up of all physical and

mental processes The neurotic retains his normal interests but frequently complains of being unable to enjoy them because of fears, obsessions and doubts The endogenously depressed patient loses some or all of his interest in things (family, radio, movies and newspapers) Insomnia is usually a more striking symptom in endogenous depressions The sudden onset of severe neurotic symptoms with a history of episodic recurrence in a previously well integrated and healthy individual is more common in the endogenous depressions We cannot confirm the observations of Watts[33] who finds the knee jerks more sluggish in depressions We have had no experience with the method of Karnosh and Gardner,[13] who use stellate ganglion block as a diagnostic measure, reporting that endogenous depressions respond favorably to the block while schizophrenic and psychoneurotic depressions do not

It is important to point out that endogenous depressions may also occur in psychoneurotics Electroshock therapy often helps in the evaluation of symptoms in such patients If neurotic symptoms disappear completely following electroshock therapy, they may be considered as equivalents of manic-depressive psychosis If they persist after the depression has cleared up, psychotherapy is recommended for the existent psychoneurosis

We studied 200 patients with depressions during a five year period, 151 women (75.5 per cent) and forty-nine men (24.5 per cent) The majority of our patients were between 35 and 45 years of age, the youngest was 16 and the oldest 70 Table 1 shows the diagnoses and the number and percentage of patients in each group, the results of treatment are shown in Table 2

All seven patients with postpartum depression (100 per cent) responded very well to electroshock therapy The response in the patients with involutional melancholia was also excellent (96 3 per cent) Of the patients with endogenous depression, 89 2 per cent improved Of those with psychoneurotic depression only 62.5 per cent responded All psychoneurotic patients were treated psychotherapeutically after the electroshock treatments, those whose depression cleared up after the electroshock therapy were more amenable to psychotherapy and responded to it much more quickly Recovery took place in 85.5 per cent of all the patients in this series

Tillotson and Sulzbach[27] studied the response to electroshock therapy in seventy patients with various forms of depression, compared with the outcome in a control group of sixty-eight untreated patients They found the improvement rate 30 per cent higher and the recovery rate 44 per cent higher in the treated than in the untreated group Improvement and recovery occurred even in chronic depressions

In many instances in which treatment had to be discontinued before

complete recovery, improvement continued without further therapy, remission apparently occurring spontaneously after being initiated by the treatment Forty-two of the 200 patients continued to improve despite cessation of treatment

Follow-up of 185 of the patients was possible for periods up to 5 years from the date of the last treatment, only fifteen patients (7 5 per cent) could not be followed We found it useful to continue seeing the treated

TABLE 1

DIAGNOSIS IN 200 CASES OF DEPRESSION

Diagnosis	Number of Patients	Percentage of Patients
Manic-depressive psychosis, depressed	119	59 5
Endogenous depression (one episode)	37	18 5
Involutional melancholia	27	13 5
Psychoneurotic depression	8	4 0
Postpartum depression	7	3 5
Depression with psychopathic personality	2	1 0

TABLE 2

RESULTS OF TREATMENT IN 200 CASES OF DEPRESSION

Diagnosis	Number of Patients	Improved		Unimproved		Failed to Return	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
Manic-depressive psychosis, depressed	119	99	83 2	10	8 4	10	8 4
Endogenous depression	37	33	89 2	2	5 4	2	5 4
Involutional melancholia	27	26	96 3	—	—	1	3 7
Psychoneurotic depression	8	5	62 5	2	25 0	1	12 5
Postpartum depression	7	7	100 0	—	—	—	—
Depression with psychopathic personality	2	1	50 0	—	—	1	50 0

patients at regular intervals for twelve months and thereafter once or twice a year Follow-up observation for long periods is indispensable in evaluating the results of any plan of therapy, relapses are thus discovered more readily

There were only two suicides in this series, both during relapses after adequate courses of treatment, when depression recurred, the patients refused further electroshock therapy

About a year ago a group of 150 psychiatrists,[9] all members of the American Psychiatric Association, warned against extramural electro-

shock treatments Our experience with office treatments, however, has been very satisfactory In this series 190 patients (95 per cent) were treated extramurally Hospitalization does not necessarily imply or insure higher standards of diagnosis or treatment Fear of being considered mentally ill and belief that admission to a hospital for psychiatric disorders is a stigma prevent many patients or their families from seeking psychiatric advice and help The relatively low cost of office treatment and the availability of members of the patient's family for supervision are additional advantages Impastato and his co workers[11] report that patients receiving electroshock therapy in the office respond better than do hospitalized patients, indicating that this may be due in part to the fact that the milder depressions are treated in the office

Not all depressed patients can be treated in the office or at a clinic Lack of reliable supervision for the entire day, previous attempts to commit suicide and resistance to treatment make patients unsuitable for office therapy We have, up to the present time, refused to treat patients over 60 years of age in the office Age, however, has been no contraindication to electroshock therapy Our oldest patient was 79 Older patients seem to tolerate the treatments very well, none of the skeletal and other complications in our series occurred in patients over 60

There is no way of predicting the number of treatments necessary in any particular case Each patient should be treated until recovery takes place Additional treatments are given if improvement is not maintained We found in a previous study[21] that 94 per cent of patients with various diagnoses recovered with five or fewer treatments Among the 200 patients in this series, ninety-six (48 per cent) recovered with five or fewer treatments One patient in the depressed phase of manic-depressive psychosis recovered completely after only one electroshock treatment, he has remained completely well for the nineteen months since treatment and is working at the time of this report Four others recovered completely with only one treatment On the other hand, another patient in the depressed phase of manic-depressive psychosis has to date received sixty-five electroshock treatments, given intermittently in series of two to four over a period of about three years The longest symptom free interval between treatments was eight weeks, the shortest, two weeks This patient had two previous episodes of depression, one of which lasted three years and was followed by a complete remission for five years He had not been given any shock therapy for the previous depressive episodes

Our 200 patients were given 1673 electroshock treatments, 1630 resulting in grand mal and only forty-three (2 6 per cent) in petit mal seizures The average number of treatments per patient was 8 37 We recently decided to give as many stimulations as might be necessary to induce a

seizure, to eliminate petit mal responses, which are considered inadequate and useless by most therapists We observed euphoria for a few hours after one petit mal response Batt[2] reported giving as many as twenty-six successive stimulations in order to obtain a grand mal reaction, we have given as many as five stimulations before such a reaction was obtained

Salzman[22] found that shock therapy decreases the length of hospitalization but increases the frequency of admission He also noted that relapses occur earlier in patients who have received shock treatment and that the greater the number of treatments given, the earlier the relapse

In comparing the duration and symptoms of previous episodes of depression for which patients were not treated with those of episodes for which they were given electroshock, most patients had a shorter and less severe depression after having been treated We too are impressed by the fact that electroshock therapy often increases the number of relapses while shortening the duration of the individual attacks of depression In one of our previous investigations we found an increase of relapses of about 6 8 per cent in patients who received more than five treatments, compared with the relapses in those who received five or less Of 138 patients in this series who had had previous untreated episodes of depression, twenty-five (18 per cent) had one or more depressive episodes after electroshock therapy Of sixty-two who had had no previous episode of depression, nine (14 5 per cent) had relapses after treatment Electroshock therapy seems to have played some role in increasing the incidence of relapses in some cases

A 29 year old woman who had been hospitalized in Rockland State Hospital for 10 months in 1935 was seen in an episode of depression in 1945, the attack being of relatively sudden onset While her husband was in the army, he had an operation on one of his knees Soon after this happened, she began to lose interest in things, became indecisive and pessimistic and showed dejection, especially in the morning Her movements slowed up, she showed very little initiative and soon lost confidence in herself, frequently making self-derogatory remarks There were no suicidal attempts although she often expressed a desire to die Her mother had committed suicide when the patient was 3 years old The patient had not received any treatments in 1935 but was given three electroshock treatments in 1945 She remained well for fourteen months when she again showed symptoms of endogenous depression She was given twelve treatments for this episode, but was in another relapse after eight weeks Further treatment was refused

Kalinowsky[12] mentioned that there is not enough evidence that symptom-free intervals between manic-depressive episodes are shortened by electroshock therapy However, even if this is true, he added, it does not diminish the value of and the necessity for active treatment. Electro-

shock therapy does shorten the duration of depressions but recurrences are not prevented

Geoghegan[7] and Meyer[17] have suggested the prophylactic use of electroshock once a month for a period of five years in all patients who have recurrent attacks of affective mental disease After two years of clinical experience with such preventive electrotherapy, Geoghegan considers it of definite value We have had no experience with maintenance regimens of this type

Some depressed patients recover after a few treatments and remain well Twenty-seven of our patients were given three or fewer treatments and remained well for periods up to twenty-eight months

Meyer records that in depressed patients who are given electroshock treatments relapses finally cease to appear, as if a long attack of depression had come to its natural end Our experience throws considerable doubt on the theory that electroshock tends to fragment depressive episodes, there seems to be no clear relation between the duration of the illness and the number of treatments needed to bring on a remission If electroshock therapy merely fragments the depressive episode, one would expect that more treatments would be necessary and relapses would be more frequent if the patient were treated during the incipient phase of the attack However, patients we treated in the very earliest stages of a recurring attack recovered with very few treatments and did not relapse for a long time On the other hand, others who had been suffering for many months and even years required many more treatments (ten or more) Every patient is in a sense unique, and therapy must be individualized, arbitrarily fixed series of treatments should not be prescribed

Extensive experience has demonstrated beyond any doubt that electroshock has a beneficial effect on all depressions It has a favorable effect even on depressions in organic brain diseases, such as general paresis, and on reactive depressions or severe grief reactions (Meyerson)[18] Patients with neurotic depressions responded very favorably and became more amenable to psychotherapy We cannot confirm the recent statement of Rickles and Polan[21] that patients with postpartum psychoses usually fail to respond to shock therapy Each of our seven patients responded promptly and remained well for relatively long periods of time After symptomatic relief of the depression, attention should be paid to the treatment of the underlying disorder A very early manifestation of a brain tumor may be an endogenous depression in a predisposed cyclothymic individual (Boestrem[5])

Careful physical and neurological examinations, as well as roentgenographic and laboratory studies, must be done before determination of suitability of patients for these treatments Contraindications for elec-

troshock therapy are recent head injuries, peptic ulcer, active pulmonary tuberculosis or lung abscess, thrombophlebitis, a failing heart, aortic or intracranial aneurysm, herniated intervertebral disk, acute infectious diseases and glaucoma All contraindications, however, are only relative, the severity of the particular psychotic reaction must be considered before a decision to postpone or refuse treatment is made It is important to balance the risk of electroshock treatments against the probable consequences of the untreated condition

A 50 year old man with active pulmonary tuberculosis and suffering with the depressed phase of manic depressive psychosis was recently treated The pneumothorax was refilled each time before treatment, and in addition the patient was given curare intravenously prior to induction of the electric current The depression completely disappeared X-rays taken before and after the treatments revealed no change in the lung condition

A 32 year old woman with a long history of multiple sclerosis and a recent exacerbation was given electroshock therapy because of a severe depression The depression cleared up completely There was no evidence of any effect of the treatment on the organic disease of the nervous system We have been unable to find in the literature available to us any mention of a similar case

Proper selection of patients unquestionably minimizes complications Only patients under 60 years of age and those who submitted to treatments voluntarily were treated in the office Patients with severe tachycardia or cardiac arrhythmias after the first treatment were advised to continue therapy in a hospital Patients with a recent history of peptic ulcer should not be treated because of the danger of severe hemorrhage even with curare Norman and Worthington[19] reported the case of a 56 year old woman with a peptic ulcer who suffered from a severe involutional depression She began to bleed from the ulcer after having received three electroshock treatments A few years ago we treated two men with severe depression who had peptic ulcers, one of whom was given curare before both electroshock treatments In each case, development of gastric bleeding necessitated discontinuation of treatment A man of 55 died of gastrointestinal bleeding one week after the termination of a course of 12 treatments

Three fractures occurred in this series of 1673 treatments given to 200 patients a compression fracture in the fifth dorsal vertebra in a man of 45, an impacted fracture of the humerus in a woman of 56 and a fracture of the scapula in a man of 42 There were also one dislocation of the shoulder, one tongue bite and one laceration of the lip

Many of the complications of electroshock therapy can be avoided by the use of proper technic Most therapists operate the machine while nurses or attendants help restrain the patient and hold the mouth gag

in place With better technic in holding the jaw we were able to eliminate all dislocations or fractures of the mandible and to eliminate tongue bite in all but one instance in more than 2000 office treatments We consider it more important for the mandible and gag to be held properly and therefore advise the therapist to do this while one of the assistants operates the machine

To avoid the skeletal complications which probably arise because of the initial severe jolting of the patient when the current is turned on, we prefer to give at least two stimulations of equal voltage in each treatment The first nonconvulsive response seems to relax the muscles of the patient while the physiological state of the brain becomes altered so that it responds more readily to the second electric stimulation Kalinowsky uses a low amount of current, about 70 volts, for the first electric stimulation, and a second stronger stimulus, which usually results in a grand mal reaction

To control the patient's movements during treatment, manual restraint or a modified strait-jacket is used We disapprove of interference with the free movement of the limbs during the treatment. We have found that the forced abduction movement of both upper extremities which occurs at the beginning of the seizure is responsible for most dislocations and fractures of the upper extremities Manual restraint was found to increase rather than to diminish the incidence of these complications About three years ago a depressed patient who incurred a dislocated shoulder during a treatment required further therapy A bed sheet tied around the chest restrained the upper limbs while permitting some free movements There were no further dislocations during treatment, which was continued despite the dislocation This method of restraint has been used for every treatment since then Rechtman and Winkelman[20] designed an apparatus consisting of a pelvic belt with a pair of forearm cuffs fastened to it, to prevent shoulder dislocations and fractures in the course of metrazol treatments by minimizing the degree of abduction

X-rays of the dorsolumbar spine are required in all patients before treatment In patients with severe osteoporosis, congenital deformities, old or recent fractures or cystic changes in the bones, curare is given before treatments We have been able to continue therapy in very depressed patients who had sustained fractures of the spine or other bones during previous treatment

We have given curare without any complications Patients requiring curare are always treated in a hospital Of the two preparations available, we prefer d tubocurarine chloride solution This preparation and intocostrin are both supplied in solutions containing 20 units per cc Given intravenously about two minutes before the electric shock treat-

ment, curare decreases the intensity of the convulsion and prevents skeletal complications The amount of curare given depends on the weight and muscular development of the patient, women usually require less than men One-half unit of curare per pound of body weight has been recommended We prefer to use smaller doses and increase the amount of curare during later treatments if necessary Before the first treatment, at least 1 cc of curare (20 units) less than the calculated dosage is given The injection is given very slowly, 2 cc of the solution in about one minute After the seizure, when curare is used, we give 1 cc of prostigmine methylsulfate 1 2000 subcutaneously or intravenously

Impastato and his co-workers[11] and others suggest the use of sodium amytal intravenously as an adjunct to electroshock therapy because of the lessening of the apprehension of patients prior to treatment, and the reduction of the incidence of fracture We have found no need for such use of sodium amytal prior to electroshock treatment Patients seem to fear the intravenous injection more than they do the electric treatment, of which they have no recollection In addition, barbiturates such as sodium amytal depress the respiratory center in the medulla and in our opinion make the treatments more hazardous

Wilbur, Michaels and Becker[30] recommend the use of atropine by hypodermic administration prior to electroshock treatments to diminish salivation and prevent aspiration We have found atropine, even when given by mouth, very helpful in diminishing salivation Use of this drug enabled us to treat without complication a woman with an involutional depression who suffered from bronchiectasis of the right lung Atropine before the treatments also occasionally seems to have a beneficial effect on prolonged apnea and irregular breathing that follow some seizures Goodman and Gilman[8] postulate that atropine has a stimulating effect on the respiratory center

Hypertension is often considered a contraindication to electroshock therapy In investigating the influence of electroshock treatments on hypertension, we found in 55 instances an immediate rise (systolic up to 80 mm , and diastolic up to 30 mm) after treatment However, the blood pressure went below the original level (diastolic as much as 30 mm , and systolic as much as 50 mm) within three to ten minutes after each treatment The highest blood pressure in one of our treated patients was 235 130 Control patients with normal blood pressure readings also showed an immediate rise of the blood pressure after treatment However, the rise in these normal controls was not as great (systolic up to 40 mm , and diastolic up to 20 mm), and pressure returned to normal within two to five minutes after treatment

Memory disturbances, some difficulty with concentration and changes in the electroencephalogram are only temporary, usually clearing up in

six to eight weeks The longest period of memory disturbance seen in our series was seven months Psychotic episodes following electroshock therapy were not observed Depression was frequently accentuated for a few minutes after the first few treatments

SUMMARY

1 Electroshock treatments are of great benefit in depressive states and their use is therefore justified

2 Electroshock therapy is superior to any other known form of treatment

3 Two hundred patients with the depressed phase of manic-depressive psychosis, involutional melancholia, psychoneurotic depression, postpartum depression and depression with psychopathic personality were treated, with an average of 8.37 treatments per patient

4 Five patients (2 5 per cent) recovered after only one electroshock treatment and remained well up to nineteen months Ninety-six patients (48 per cent) improved with five or fewer treatments One patient with a recurrent depression has received sixty-five electroshock treatments and is still under observation

5 All the patients with postpartum depression recovered (100 per cent), improvement occurred in 96 8 per cent of the patients with involutional melancholia, 89.2 per cent of those with endogenous depression, and 83 2 per cent of the manic depressive patients Of the entire group of 200 patients, 171 (85 5 per cent) had complete remissions for periods up to five years

6 Thirty four (17 per cent) of the 200 patients have had one or more relapses following electroshock treatments Fifteen (7.5 per cent) failed to return and could not be followed

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TREATMENT OF CHRONIC FORMS OF MALIGNANT LYMPHOMAS AND LEUKEMIAS

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WHEN one contemplates the range of problems involved in the treatment of the malignant lymphomas and leukemias the first and lasting impression is one of enormous complexity Each of these diseases—Hodgkin's disease, lymphosarcoma, reticulum cell sarcoma and the leukemias—possesses in itself numerous complexities, since any organ or tissue whatsoever may become affected by any of them They are notoriously capable of wide variations, and certain apparent transitions from one to another not infrequently occur Although patients of certain age groups predominate in various of these diseases, in general no age is immune, and the conditions are of particular sociologic importance because to such a large extent they affect persons in the younger age groups and those in the prime of life The chronic forms characteristically produce a long period of invalidism in the patient, with such a multiplicity of symptoms and signs that the ingenuity of the physician is taxed to the utmost to provide proper care

These diseases so universally regarded as lethal comprise a considerable proportion of all cancer Figures from New York City show that they account for about one in every sixteen deaths from cancer A recent study indicated that the incidence of leukemia may be increasing

The general approach to the problem of treatment of the chronic forms of malignant lymphoma and leukemia may be considered relatively simple, although the actual details of treatment in any individual case are almost invariably extremely complex The relatively simple general approach consists primarily in a determination of which one of three categories, in regard to extent of the disease, is the one that fits the particular case at hand These three categories are (1) the early, strictly localized disease, (2) the intermediate stage of spread of the disease, and (3) the stage of marked generalization of the disease The last category of course includes all leukemias

Evidence available today offers a distinct hope for salvage in the early case with strict localization of the disease, that is, in early Hodgkin's disease, lymphosarcoma, reticulum cell sarcoma and a few cases of apparently localized mycosis fungoides There should be hope for better

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control in the intermediate cases and perhaps even hope for better palliation in the generalized cases

Choice may now be made among many more methods of treatment than were available ten years ago Irradiation from external sources remains by and large the therapeutic agent of widest applicability and effectiveness External irradiation nowadays is chiefly by means of x-rays, radium seldom being used for external irradiation chiefly because, depending on the mode of its use, it is cumbersome, inconvenient or uneconomical

X-rays may be used in a wide variety of methods, voltages ranging from 50,000 to 1 million or more depending on the lesion to be treated, and the size of field treated varying from as little as 1 cm in diameter to a large field encompassing the entire body

In this field of diseases there is seldom need for intracavitary or interstitial employment of radon or radium Internal irradiation, however, in the form of radioactive isotopes for treatment of the entire body from within, has become widely employed in the last decade Some of these isotopes may be somewhat selective for the malignant tissue, others having no selectivity confer a type of irradiation analogous to whole body x-ray treatment

Chemotherapy is not new in the treatment of these diseases The use of arsenic has a long history with some revival of popularity, particularly in the last fifteen years, in the treatment of leukemia Benzol has a long history, but in this country has largely fallen into disfavor in the treatment of leukemia Since late 1942 nitrogen mustard has come into widespread use, particularly in this country, in the treatment of all these diseases, finding its greatest field of usefulness in the treatment of Hodgkin's disease In the last two years urethane has had a certain vogue, particularly in the treatment of leukemia Stilbamidine has been tried fairly widely in the treatment of plasma cell myeloma The sodium salt of para-aminobenzoic acid has been tried, but without much success In the last few years various so-called anti-folic acid preparations have attained considerable prominence in treatment of leukemia and have shown interesting results but, unfortunately, no promises as yet of cure Some attempts have been made to use various hormones, but so far no series of striking results has come to light

Surgery has a limited application in the removal of early, localized, accessible malignant lymphoma

In the adjuvant methods of treatment newer knowledge has added considerably to their effectiveness The uses and risks of blood transfusion are better known Much has been learned about the uses and risks of plasma administration The significance of alterations in blood chemistry is becoming better understood The refinements of radiologic diag-

nosis have added materially to the detection of those obscure lesions which often mean so much more to the morbidity and even to the mortality of the patient than do the more obvious superficial or readily detectable lesions

Insofar as possible, diagnosis must rest on biopsy of material obtained by one means or another Far too many cases are allowed to go undiagnosed, or treatment is given without proof of diagnosis, and in most of them reasonably early proof of diagnosis by some method of biopsy is possible It cannot be denied, however, that in some early obscure cases the diagnosis remains a puzzle until the disease is considerably advanced This statement applies in some degree to all the members of this group of diseases

HODGKIN'S DISEASE

The Early Case.—Numerous cases can be picked out of any large series demonstrating the principle that at least to a considerable extent Hodgkin's disease begins in one focus and spreads from there If the disease is detected while it is still in its early stage and if the initial focus is accessible for surgical removal, the question may always be raised whether the initial treatment should be by radical surgical intervention Actually of course, in present-day practice, such strict localization of the disease is rarely seen It must be admitted that the evidence for the application of this principle of treatment rests mostly on past experience in the observation of certain patients with localized disease who were treated fairly early, either by surgery or by irradiation or both, with long subsequent survival and an obvious tendency, even though spread occurred later, for the disease to remain relatively regional for a long time

There is as yet very little experience in cases in which surgical intervention was deliberately chosen in the early localized state of the disease In some cases at Memorial Hospital in the last few years, in which an attempt has been made to eradicate the disease by surgical removal of an apparently single accessible focus, the results have been rather disappointing in that evidence of further spread of the disease appeared before long In some of these cases the disease was probably too near the borderline of suitability for operation Moreover, considering the cellular nature of the process, it has always seemed to me that it would be improper to rely on surgery alone, and that surgical intervention should be followed by moderately heavy irradiation of the region Moreover, it is still a question whether it might not be better to accept the undesirable late effects of radical irradiation—fibrosis and telangiectasis, because it is not yet established that radical irradiation may not actually

offer a better chance for complete control of the disease than does surgical intervention with its hazard that incisions might actually be crossing tumor-bearing tissues

Such reports as those of Slaughter and Craver (1942), Gall (1943) and Hellwig (1947) lend support to the belief that adequate early treatment of a localized early process may offer hope for cure

There has been no determination of what constitutes a sufficient dose of irradiation to destroy the process in early localized Hodgkin's disease Probably this dose varies widely from one patient to another It seems certain that one should not be contented with delivering just enough irradiation to produce regression In all likelihood a sufficient dose will approach the maximum dose that can be tolerated by the skin overlying the affected area It is not clear whether it is desirable to attain this maximum dose by multiple small fractions spread over a few weeks or whether in some cases it might not be preferable to deliver larger fractions, a method which because of the limits of skin tolerance, would necessitate restriction of the total dose to a smaller amount, delivered over a shorter period of time There seems little doubt that if dosage is restricted in the early localized case to that amount which is just sufficient to cause regression, it will be only the rare, extremely radiosensitive and atypical case that will show a permanent remission It may seem strange that this matter of requisite dosage has not been determined before now The reason for this lack of knowledge is that in treating Hodgkin's disease almost all of the effort must, unfortunately, be directed toward the treatment of patients who already have more or less spread of the disease and who therefore, in consideration of their welfare, cannot properly be subjected to experimentation to determine the sterilizing dose for one or more of the multiple foci of the disease

Another therapeutic agent which has been found useful for palliation in Hodgkin's disease would seem, at present at least, to have no place in the care of the patient with early strictly localized Hodgkin's disease It would seem most undesirable to subject the entire body to the toxic action of nitrogen mustard when one is seeking to abolish a single focus of Hodgkin's disease However, considering the possibility that many patients with apparently early disease localized in one focus may actually have much more widespread granulomatous foci than is suspected, and if one assumes that nitrogen mustard possesses the capability of permanently destroying small early foci, although as yet there is no evidence of such a possibility, one might argue that nitrogen mustard, as well as local x-ray therapy, should be employed in apparently early cases

In deciding what patient actually has an early localized process it would seem well to keep in mind the thought that what seems to be an early manifestation may actually be only a signal of a process that has

begun somewhere else and has spread to the region in which the disease first becomes manifest For example, Hodgkin's disease apparently localized to the inner part of the supraclavicular region may actually be secondary to a primary focus in the region drained by the thoracic duct, even though no evidence of disease may be demonstrable in the mediastinum or abdomen The same general consideration applies to early Hodgkin's nodes found in the axilla or in the groin Quite often in such cases it is only a few months before the disease becomes evident in an area from which spread to the region where the disease first became manifest could readily have occurred by way of the lymphatics

When Hodgkin's disease begins, as it not infrequently does, in some deep internal focus, particularly in the abdomen, early diagnosis may be quite impossible, and such cases are likely to remain diagnostic puzzles until the disease is no longer in the early state With greater development of diagnostic acumen more of those cases may be discovered early and the diagnosis, particularly in those with abdominal lesions, may be proved in the course of exploratory operation Then with the prompt application of adequate surgical intervention or irradiation, or both, even some of these patients may be salvaged, at least in terms of long survival, if not in terms of cure

The Intermediate Stage.—In the majority of cases of Hodgkin's disease, by the time the diagnosis is made the process has already reached an intermediate to an advanced stage, precluding the possibility of cure by any means known today It is still worth while, however, to classify the case as to whether it is in an intermediate stage with relative regional localization of the process, or whether it has become universally generalized The intermediate stage of Hodgkin's disease, in which the disease is found in a few contiguous regions, for example in the mediastinum and supraclavicular regions, will merit consideration of fairly aggressive treatment, because a good many such cases are susceptible of control for long periods and may even for many years remain free of evidence of relapse In this type of case, too, it appears that irradiation with x-rays remains the primary treatment of choice Experience would indicate that nitrogen mustard is extremely unlikely to produce an apparent complete disappearance of the disease in such cases as this, with perhaps few exceptions, whereas it is not at all an uncommon experience to see, after adequate irradiation, apparent complete disappearance of all evidence of the disease for variable periods of time, depending on the aggressiveness of the process Here again if just sufficient treatment is used to bring about remission, the chances for any long salvage will be minimal, except in the extremely rare type of case in which the process is extremely radiosensitive On the other hand, in some such cases, evidence of reactivation or further spread of the disease may appear early This

makes it obvious that one is dealing with a type of case in which the disease is naturally more aggressive, and therefore that one must begin to think of that case as belonging in the last category, in which universal generalization will shortly take place, and in which efforts at therapy must of necessity be confined to treatment of the more important signs or symptoms, recognizing then that overly aggressive treatment may do more harm than good

In the lymphoma clinic at Memorial Hospital, when a patient with Hodgkin's disease presents mediastinal nodes and bilateral supraclavicular nodes, the current practice is to begin treatment by a course of x-ray therapy outlined usually as follows treatment ports are marked out over the mediastinum anteriorly and posteriorly, usually a single port anteriorly and one posteriorly, sometimes two oblique ports anteriorly and two oblique ports posteriorly, to be treated at a 70 cm target distance with the 250 kilovolt x-ray machine, and ports are outlined for each supraclavicular and lower or entire cervical region as may be required for adequate inclusion of the enlarged nodes in those areas If the general condition of the patient indicates that he may be able to tolerate irradiation fairly well, it has become customary to treat one mediastinal field and one supraclavicular-cervical field together in one day, giving each field usually about 200 r The supraclavicular-cervical field is treated at either 50 or 70 cm distance, depending on the thickness and depth of the node mass in the region One mediastinal and one supraclavicular field will be treated one day, the other mediastinal and the other supraclavicular field the next day In this manner the treatment proceeds, with exposure of two ports each day until each port has received a minimum of 1800 to 2000 r, measured in air Various circumstances may necessitate modifications of this plan The more ill patient may require hospitalization during treatment, or it may seem desirable to treat only one port a day To do so, of course, would require double the length of time in order to complete the entire cycle The individual dose administered to each port may be decreased or somewhat increased, depending on the estimate of the patient's ability to tolerate irradiation, an estimate made either initially or after the trial of a few treatments

In this intermediate type of case with relatively regional localization of the disease the question may always be raised whether irradiation should be preceded by use of nitrogen mustard It would seem that this a question which cannot be answered categorically In many patients the administration of nitrogen mustard may be followed by such a degree of leukopenia that it appears unwise to administer the full amount of x-ray treatment originally planned, or even to give any at all It may be stated as a general rule that recovery from leukopenia, after the use of

nitrogen mustard, may occur even when a course of x ray treatment is begun immediately after the course of nitrogen mustard, provided the volume of body tissue irradiated is not too large Individual factors of susceptibility to the leukotoxic effects of nitrogen mustard and of x-ray therapy play a large part here In general, confronted with a patient such as the one cited in the example above, with mediastinal and bilateral cervical and supraclavicular nodes, I would prefer to start the treatment by x-ray therapy, and to reserve nitrogen mustard for possible later use

In regard to the better sequence of use of nitrogen mustard and x-rays, clinical and some experimental evidence suggests that if the two are to be used together, that is in sequence, it is preferable to use nitrogen mustard first Some efforts have been made and others considered toward use of a single massive dose of nitrogen mustard immediately followed by a single massive dose of x-ray treatment. In the case of mediastinal Hodgkin's disease, however, this would seem to be a rather risky method of treatment, considering particularly the danger of irradiating the mediastinal mass in a single large dose There seems to be less danger of asphyxial reactions from mediastinal tumors after use of nitrogen mustard than there is after the use of large doses of x-rays It should be added that whenever a mediastinal tumor is bulky or produces respiratory embarrassment it is desirable to start the irradiation very cautiously It has commonly proved to be a good plan to give a single small dose anteriorly to the mediastinum as a test of the likelihood of an asphyxial reaction of greater or lesser degree, and then to wait two or three days to let the reaction cool off, so to speak, before proceeding with further treatment This initial dose to the anterior mediastinum may vary from 50 to 100 r, and in some cases when treatment is resumed after a pause of two or three days the doses to the mediastinum are stepped up gradually until it seems safe to proceed with the full single dose that has been decided on

The Stage of Generalization—When examination indicates that Hodgkin's disease has become quite generalized, one can seldom hope for long control of the condition A survey must then be made to indicate which are the more important regions to be treated In this type of case, in which the patient is more commonly toxic, with chills, fever, night sweats, itching and often pain, the quickest palliation may often be accomplished by nitrogen mustard injection Nitrogen mustard may detoxify such a patient within a few days, bringing about a drop in temperature to normal or nearly normal, more or less regression of the enlarged nodes, spleen, etc , and this detoxification may be accompanied by a marked general improvement in the patient's sense of well-being, and a marked gain in appetite and in functional capacity In some such

cases the result after injection of nitrogen mustard has been so good that the original plan to follow its use with administration of palliative doses of x-rays to various areas has been abandoned

One of the most important things to recall in considering any case of Hodgkin's disease is that any tissue may be affected Symptoms referable to the respiratory, gastrointestinal or urinary tract, the osseous or nervous system, or any other tissue demand investigation to determine whether they are caused by lesions of Hodgkin's disease As stated before, these deep and often obscure lesions may be of much more importance to the morbidity and even to the mortality of the patient than are the more obvious enlargements of lymph nodes and spleen It is essential to search them out and to devise appropriate treatment for them Such lesions, when discovered, should be regarded not as terminal manifestations but as indications for appropriate treatment For example the onset of paraplegia need not be regarded as heralding a terminal state of the disease Prompt determination of the level at which the cord is affected, and prompt and adequate treatment, may result in disappearance of the paraplegia, permitting the patient to live for several years Lesions of the lungs not infrequently can be more or less completely cleared up by adequate treatment Even large lesions of the stomach, causing pain and hemorrhage, may be made to disappear Lesions of bones have been seen to heal after x-ray therapy Nitrogen mustard does not seem to have had a very satisfactory effect in general on lesions of the bones in Hodgkin's disease

LYMPHOSARCOMA

Considering under the broad term lymphosarcoma the various conditions designated as giant follicular lymphoma, lymphocytic lymphosarcoma, reticulum cell sarcoma, and lympholeukosarcoma, we are confronted with a markedly variable and complex group of disorders Giant follicular lymphoma is characteristically an extremely radiosensitive disease Usually when it is discovered, the patient presents a more or less generalized enlargement of lymph nodes, together with enlargement of the spleen and frequently of the liver, but may be in fairly good general condition If the biopsy of a peripheral node diagnosed as giant follicular lymphoma truly reveals the entire process, the response to moderate doses of x-ray irradiation may be remarkable All evidence of the disease may disappear and the patient may remain well for years In other cases it seems likely that the biopsy of the peripheral node does not reveal the entire process, because one may find that, although some of the nodes disappear rapidly, others are more radioresistant, or relapses may occur in a few months Although giant follicular lymphoma is often

said to be an initial stage of reticulum cell or polymorphous cell sarcoma, of Hodgkin's disease, or of lymphatic leukemia, the experience at Memorial Hospital has indicated that in the great majority of these cases the condition sooner or later is converted to full-blown reticulum cell sarcoma, becoming also less radiosensitive and more aggressive In not a few cases there has been a concomitant blood picture of chronic lymphatic leukemia, and in a very few a later biopsy has revealed a condition interpreted as Hodgkin's disease

Taking as an example of a typical case a patient in his thirties who presents enlargement of cervical, axillary and inguinal nodes, a rather bulky deep central abdominal mass of retroperitoneal nodes and an enlarged spleen, but who nevertheless remains in fairly good general condition, with few constitutional symptoms, the first decision is whether treatment should be by nitrogen mustard or by x-rays In general, the effects of nitrogen mustard therapy in a limited group of cases of this type have been somewhat disappointing X-ray therapy in such a case would be outlined about as follows a single dose of about 300 r measured in air would be given to each of the peripheral node masses, treating one field a day, or one every other day, and the central abdominal mass would be outlined for treatment through either a large single oblong field anteriorly and posteriorly, or perhaps an upper and a lower anterior and an upper and a lower posterior field These fields would receive something in the order of 200 r to one or two of them a day until a total of 400 to 600 r per field had been reached If the entire process is actually one of giant follicular lymphoma, such a course of treatment may be followed by complete or nearly complete disappearance of all palpable evidence of disease If the spleen is very large it may be treated also in doses usually not exceeding 100 r to one port a day, carried up to a maximum of usually not over 300 or 400 r per port After such a course of treatment the patient is observed at regular intervals of three to six weeks, and upon the discovery of any evidence of enlargement of a new node group, or of re-enlargement of a node group previously treated, further treatment is given Naturally it is impossible to lay down any general rule to apply to all these cases, as in this entire field, individualization of treatment is necessary

One may draw inferences regarding the progression of giant follicular lymphoma toward full-blown reticulum cell sarcoma from the biopsy reports of pathologists in cases which would seem to have started as giant follicular lymphoma Judging from these biopsy reports one can visualize the progression as follows giant follicular lymphoma, follicular lymphoma becoming diffuse, follicular lymphosarcoma, lymphosarcoma with follicular traces remaining, reticulum cell sarcoma

Although in general reticulum cell sarcoma tends to be more aggressive

and more radioresistant, it too shows a wide variation in its response to irradiation (It should be noted here that there is considerable variance in what different pathologists designate as reticulum cell sarcoma) At Memorial Hospital some lesions which on biopsy are reported to be reticulum cell sarcoma have been extremely radiosensitive, others have been intermediate in their response, and others have been markedly radioresistant Particularly noteworthy have been certain skin tumors somewhat resembling mycosis fungoides clinically, but reported as reticulum cell sarcoma, which have shown complete local remission for long periods after adequate irradiation

Whenever localized lymphosarcoma is accessible for surgical removal the question may always be raised whether surgery or irradiation is the treatment of choice Here again, as in Hodgkin's disease, results of radical surgical removal have sometimes been disappointing, and the question may be regarded as still open whether the objective of complete control of the local disease might not be better attained by radical irradiation, even though one would have to accept the undesirable late effects For reticulum cell sarcoma, apparently primary in one bone, although early amputation has been advocated by the Boston group, control for long periods has been observed after irradiation Catlin's recent survey of lymphosarcoma primary in the head and neck region shows a five year survival rate exactly double that reported for lymphosarcoma in general by Stout and by Craver No doubt most of the single lymphosarcomatous tumors of stomach or intestine, if amenable to surgical removal, are better treated by that method than by irradiation alone

Lymphosarcoma in children in general tends to be a rather acute process and not infrequently is sooner or later accompanied by a picture of acute leukemia Therefore these cases do not come within the range of the present discussion

Chronic Leukemia.—In discussing treatment of chronic leukemias we are concerned almost entirely with chronic myeloid leukemia and chronic lymphatic leukemia Most cases which may be regarded as monocytic leukemia, whether one considers them to be true monocytic leukemia or monocytoid forms of myeloid leukemia, tend to have an acute or subacute course and their treatment is essentially no different from that of the other acute or subacute forms Leukemia in children is nearly always acute or subacute Rarely somewhat chronic forms appear in children and may be treated essentially as in the adult

The typical case of chronic myeloid leukemia, presenting an enlarged spleen, no enlarged peripheral nodes, often an enlarged liver and few or no blasts in the peripheral blood and only a few blasts in the marrow, usually responds well at first to treatment of the enlarged spleen by x-rays Treatment of the long bones by x-rays has seemed less effective

and somewhat more hazardous because of danger of a rapidly developing anemia Obviously the treatment of the spleen in such a case is, in a way, merely treatment of a sign of the disease, yet, curiously, such treatment seems in general to work pretty well in a palliative way

Benzol is seldom used any longer in this country for the treatment of chronic leukemia Arsenic, if pushed to the limit, may produce a remission, but usually the dose of arsenic required is such as to cause undesirable side effects At Memorial Hospital the use of arsenic has been restricted in the main to two purposes (1) as an initial course in moderate doses (usually not exceeding 5 or 6 drops of Fowler's solution three times a day) in cases in which, when they are first encountered, there seems to be some tendency toward acuteness, so that one is somewhat hesitant to begin immediately with the usual cycle of x ray treatment to the spleen, (2) as an agent employed occasionally for maintenance therapy

For the ambulant patient with typical chronic myeloid leukemia, x-ray treatment to the spleen is usually given in divided doses of 50 to 100 r, measured in air, at a 70 cm distance to one field over the spleen anteriorly and one field posteriorly, unless the spleen is so large that it seems advisable to divide the anterior and posterior fields into two or possibly more ports each When the spleen is somewhat smaller it may be treated through a single circular field directed laterally over the spleen In other cases in which the spleen is somewhat elongated and it seems undesirable to permit the beam of radiation to penetrate to any great extent into the rest of the abdomen, a trial has been made of devising a circular field over the lower pole of the spleen and over the upper pole, with a specification that the beam of x-rays shall be directed so as to pass along the long axis of the spleen, thus, so far as possible, confining the beam to the region of the spleen alone

A favorable response in a typical case of chronic myeloid leukemia to treatment by means of x rays delivered to the spleen may consist in a marked shrinkage of the spleen within a month or six weeks, along with a restoration of the blood count to nearly normal Not infrequently an increase of 1 million red blood cells has been observed within three or four weeks without benefit of transfusions or hematinic medication

When, aside from arsenic, the only effective treatment for chronic myeloid leukemia was external irradiation, the patient who had little or no enlargement of the spleen or liver when first seen presented a problem as to where to administer x-rays Irradiation of the entire body, of large sections of the body, of some field such as the thorax, or perhaps, reluctantly, of the bones might be tried Since the advent of radioactive phosphorus a case of chronic myeloid leukemia such as the one just described has seemed particularly suitable for the somewhat selective total

body internal irradiation afforded by that agent As a rule, when the patient with chronic myeloid leukemia presents a considerably enlarged spleen it has not seemed desirable to begin the treatment with radioactive phosphorus Even in some cases in which the spleen has not been greatly enlarged and in which radioactive phosphorus has been used, it has seemed at times advantageous, when a relapse occurred, to irradiate the relatively small spleen through a circular direct lateral port Since radioactive phosphorus became available in the practice at Memorial Hospital, most patients with chronic myeloid leukemia have received at one time x-ray therapy and at another time radioactive phosphorus, depending upon the various conditions

The administration of urethane, by mouth if possible, or by intramuscular or intravenous injection, may bring about a satisfactory remission in some cases of chronic myeloid leukemia Urethane seems somewhat undependable With doses adequate to produce a remission the patient may complain considerably of gastrointestinal disturbances, chiefly loss of appetite, nausea and occasional vomiting The doses commonly used have ranged from 2 to 4 gm a day, but in some cases 9 to 12 gm a day has been tried These larger doses nearly always cause gastrointestinal upsets Urethane is not entirely without danger There have been some observations of toxic effects on the bone marrow

Injections of nitrogen mustard may produce remission in chronic myeloid leukemia but there has been no evidence of superiority of this treatment over x-ray therapy

Considerable interest has recently been aroused in certain so-called anti-folic acid compounds, such as aminopterin, amethopterin and amino-an-fol These compounds have been of interest particularly because of their effects in producing temporary remissions in some cases of acute and subacute leukemia in children In a few cases of acute leukemia in adults they have had transitory, rather slight beneficial effects In chronic leukemia there is little evidence so far that they should supplant the older therapeutic agents such as x-rays and radioactive phosphorus They may be toxic, and unpredictably and dangerously so

It is of considerable advantage that we now possess a choice of methods of treatment of chronic myeloid leukemia In some cases when one method seems to be failing another method may temporarily bring about improvement

When enlarged nodes or a bone lesion develops in a patient who has previously had chronic myeloid leukemia, one is rather safe in concluding that the disease will be more aggressive and more acute than before

Chronic Lymphatic Leukemia—The typical case of this disease presents a rather uniform enlargement of lymph nodes, usually less enlargement of the spleen than in myeloid leukemia, and some enlarge-

ment of the liver In treatment of such a case by x-rays it is often useful in the first course to treat mainly the enlarged peripheral nodes, sometimes the retroperitoneal nodes as well, if they are readily palpable This course of treatment of the more accessible and more obviously enlarged nodes, in a favorable case, not infrequently results in a marked regression of the enlarged nodes and a marked restoration of the blood count toward normal, accompanied by improvement in the patient's general condition Such a course of treatment may consist of 100 to 200 r once around to ports suitably designed to include the node groups that one has decided to treat Depending on the response, after a suitable time further treatment may consist of irradiation of the deeper lying node masses or deeper node regions, such as the mediastinum, and perhaps the spleen and liver

Some patients with chronic lymphatic leukemia, as far as objective findings are concerned, present chiefly a huge spleen that might lead one to think at first that the case is one of chronic myeloid leukemia In such event the spleen, being regarded as the chief repository of leukemic tissue, would be treated first, much as in the case of chronic myeloid leukemia Other patients with chronic lymphatic leukemia may present little if any enlargement of nodes anywhere, as far as one can determine by palpation or by roentgen films of the chest In such event one may still choose to treat the lymph node-bearing regions or to resort to spray x-ray therapy or total body x-ray therapy Some have come to favor spray therapy as the method of choice for irradiation in chronic leukemia

Radioactive phosphorus may produce rather good remissions in chronic lymphatic leukemia, although as a general rule they are not as satisfactory as in chronic myeloid leukemia and no better than the remissions produced by x-ray treatment

In chemotherapy of chronic lymphatic leukemia arsenic is generally regarded as having not as good results as in treatment of chronic myeloid leukemia Urethane may be useful at times in chronic lymphatic leukemia Nitrogen mustard may produce remissions in this disease It has been of interest to note that in a few cases of so-called lympholeukosarcoma—that is, cases in which the biopsy is reported as lymphosarcoma, although the blood count shows a picture of lymphatic leukemia—the results of nitrogen mustard therapy have been striking, and rather long lasting The use of the so-called anti-folic acid preparations in this disease is apparently less desirable than the older methods of treatment

Adjuvants to Treatment.—If one tries to do the best possible in the way of palliation in cases of the chronic forms of lymphoma and leukemia much more is required than the mere application of one of the specific methods of treating the disease itself Patients with these dis

cases are more or less chronic invalids Above all they need encouragement, and attention to their living conditions and to the amount of sleep and rest that they have At least in the beginning it is better not to inform the patients regarding the true nature and prognosis of their disease When they are treated in an institution where many other patients with the same diseases are treated they will inevitably sooner or later find out the name of the disease from which they are suffering This discovery may cause considerable discouragement, and the physician should be alert to give what reassurance he can It is not an absolute rule that no patient should be told the nature of his disease in the beginning, but as a general policy it has seemed far better to minimize to the patient the seriousness of his disorder The nearest relative or responsible person should of course be informed

Attention must be paid to nutrition It would seem that the value of vitamin therapy may have been considerably overstressed I have not been much impressed by the value of loading these patients with vitamins, nor is iron usually prescribed unless the blood picture indicates an iron deficiency There is much more resort to transfusions nowadays than formerly in combating severe anemia, but it must be recognized that transfusion reactions seem to be of much more common occurrence in patients with these disorders, especially when multiple transfusions are given

Antibiotics have come to play a considerable part in the treatment of the febrile state in these conditions, although for the most part their use is rather empirical Those who have recurrent bouts of fever accompanying generalized malignant lymphoma or leukemia seldom have positive blood cultures or show any distinct evidence of focal infection, yet not infrequently one of the antibiotics may abolish fever The antibiotics are often tried empirically in turn, first penicillin and then streptomycin, and finally as a last resort one of the sulfonamides

The local use of antibiotics for local infections, as in ulcerative mouth lesions, may completely alter the picture presented by such a complication

SUMMARY

In summary, the chronic forms of malignant lymphoma and leukemia constitute a wide range of diseases which should be primarily the concern of the internist, who in the management of the complex diagnostic and therapeutic problems that arise may need the cooperation of the surgeon for obtaining biopsy specimens and sometimes for treatment, of the pathologist for diagnosis, of the roentgenologist for diagnosis and therapy, and of almost any other kind of specialist, in view of the multitude of lesions and symptoms that may arise

THE ANEMIC STATES THEIR CAUSES AND TREATMENT

CHARLES A DOAN, M D, F A C P * AND CLAUDE-STARR WRIGHT, M.D †

PRIMITIVE man recognized objective pallor and subjective coldness as associated with "bloodlessness," and his empiric belief in the dependence of the "life principle" upon the blood was entirely logical Better to understand the nature and control of these anemic states, man has passed from the mystic concepts and descriptive terminology of yesterday, to today's objective inquiry of basic mechanisms through controlled experimentation. To the extent that basic hematologic knowledge has abundantly accrued in recent years, we are now able to distinguish the precise cause and apply the specific treatment in most of the patients with anemia While there are still incompletely understood aspects of this ancient symptomatic cryptogram, so many of the facts involving the hemolytopoietic equilibrium have been revealed that success in blood cell re-equilibration today is far more frequent than failure

It is probable that anemia is the one sign most commonly encountered by physicians in patients of any age, particularly in long-term illness It may be the result of a primary defect in the hematopoietic tissues, but more frequently it bears a secondary though important symptomatic relationship to some other disease syndrome *Precise diagnosis must precede the selection and application of specific therapy* Knowledge of the basic facts relating to human erythropoiesis, as at present understood, is essential to intelligent diagnosis and treatment

NORMAL ERYTHROPOIESIS

An analogy may be drawn between normal red cell formation in the bone marrow and a factory production or assembly line (Fig 157), First, the endothelium of the nonpatent, intersinusoidal capillaries is differentiated into the earliest intravascular primitive erythroid cell, the megaloblast [1] The best environment for this initial differentiation includes an area of low oxygen tension, ideally supplied in normal bone marrow For cellular development very specific materials are necessary at the various maturation levels The synthesis of hemoglobin by the megaloblast re

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quires an active "erythrocyte maturation factor" (EMF) found stored most abundantly in the normal liver Stomach, kidney, brewer's yeast, synthetic pteroylglutamic acid (common to both liver and yeast, asfolic acid, in nature), vitamin B_{12} (a cobalt complex isolated from liver),[2,3] and thymine[4] can all affect this megaloblastic maturation Proteins,[5] the amino acid glycine particularly,[6] are necessary to furnish the globin part of the molecule and protoporphyrin synthesis Inorganic iron is essential to the protoporphyrin ring in forming the hemoglobin molecule This reaction is catalyzed by trace minerals which include copper, cobalt and possibly zinc Abundant vitamin C and adequate thyroxin are apparently essential to normal erythropoiesis but their precise role in this mechanism is not entirely understood The normal mature erythrocyte

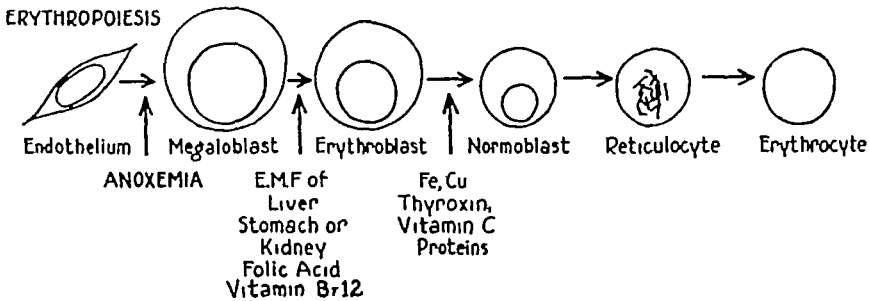

Fig 157 —In the maturation of the red blood cell from the primitive endothelium of the intersinusoidal capillaries in the bone marrow, certain metabolic "raw materials" are necessary at specific stages of the process Anoxia stimulates the endothelial differentiation into the earliest erythroid cell, the megaloblast. The "erythrocyte maturation factor" is necessary for the maturation of the megaloblast to the erythroblast Iron, copper and essential proteins are requisite to proper hemoglobin formation The unavailability of any of these materials may result in anemia

which results from this maturational "assembly line" is delivered on demand from its erythropoietic capillary focus in the marrow to the peripheral circulation where it functions as an oxygen–carbon dioxide carrier for approximately 120 days—the estimated average life-span of a normal mammalian non-nucleated erythrocyte[7]

NORMAL ERYTHROPHAGOCYTOSIS

The normal fate of the red blood cell, and the physiologic mechanism by which its important constituents are conserved for re-utilization, marks another important chapter in current hematologic investigation Both in vivo and in vitro observations have revealed and emphasized the importance of erythrophagocytosis by the reticuloendothelial cells in the removal of senile and debilitated cells, thus serving to clear the

circulating blood of its aging, damaged, inferior and fragile population The unique circulation of the spleen, its contractile muscular capsule and its normally high complement of reticuloendothelial phagocytes make this organ particularly well adapted to its well recognized physiologic reservoir and phagocytic functions for all circulating blood elements The constant finding of phagocytized red blood cells in the clasmatocytes of the normal spleen is responsible for its having been described as the physiologic "graveyard of the red blood cells " Intravascular fragmentation[8] and hemolysis have been among other hypotheses suggested to explain the physiologic turn-over in red cells

This erythropoietic equilibrium thus depends on two reciprocal variables—the actual cell delivery which reflects under duress the potential productive capacity of the bone marrow on the one hand, and the immediate peripheral demand on the other Anemia results when a negative balance develops between red cell supply and demand

THE ANEMIAS OF CENTRAL BONE MARROW ORIGIN

Inadequate or defective erythrocyte production may be caused by one or more factors working singly or in combination (1) an inherent genetic defect, as in sickle cell or Mediterranean anemia, (2) a mechanical replacement (myelophthisis) of normal erythroid elements by malignant metastases to the marrow, by leukemic cell hyperplasia, or by fibrous or osseous marrow replacement, (3) toxic cellular inhibition or destruction with functional hypoplasia, and (4) deficiency of essential materials necessary for adequate maturation

Inherent Genetic Defect.—Both sickle cell anemia and Mediterranean anemia are transmitted as a mendelian dominant trait In sickle cell anemia the fault is in the red cell stroma The trait is present in approximately 12 per cent of the Negro race Anemia due to excessive intravascular sickling is present only in 2 5 per cent of those inheriting the trait[9] Mediterranean anemia is thought to result from a fundamental defect in the ability to utilize iron in the metabolism of hemoglobin Iron therapy, blood transfusions and splenectomy have all proved to be of no permanent benefit in either disease The severity of the symptoms reflects the individual inheritance plus changing environmental factors

Myelophthisic Anemias.—Anemia may be one of the first clinical manifestations when the bone marrow compartment is encroached upon by the pathologic invasion and proliferation of abnormal cell types This displacement of normal erythropoiesis may be due to malignant metastases, leukemic cell infiltrations or fibrous tissue or osteoblastic replacement of the normal marrow elements This mechanism should

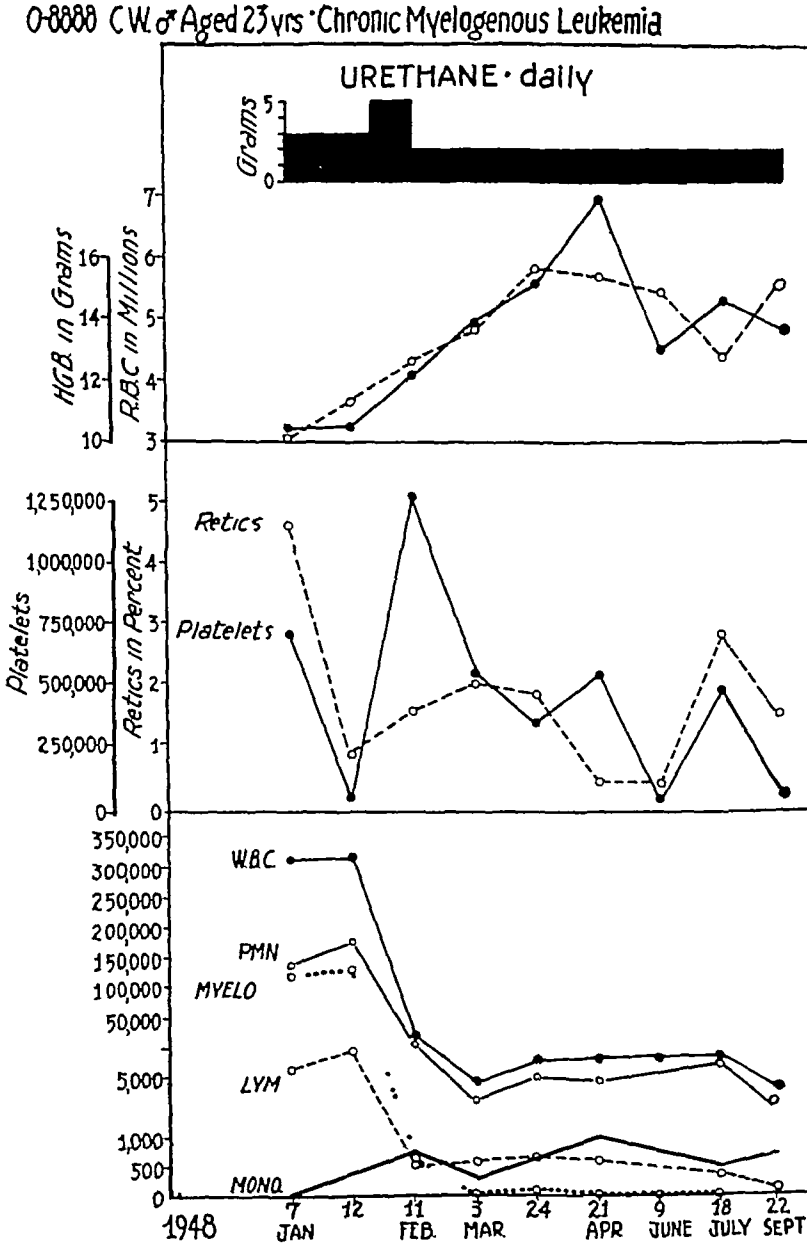

Fig 158 —Note the reciprocal rise in the red blood cell count and hemoglobin as the total white blood cells fell under urethane therapy alone The splenomegaly has diminished markedly and the marrow has returned to normal The patient is in hematologic equilibrium and entirely asymptomatic on maintenance dosage at the time of this report, ten months after the inauguration of therapy Similar "remissions" have been accomplished lasting as long as twenty months in other patients with a similar mechanism

always be suspected when a few normoblasts and/or myelocytes are seen in studies of the peripheral blood It may usually be verified and the specific cell type identified by microscopic examination of a speci-

men of bone marrow obtained by aspiration or other means Treatment must be directed against the invading cells

To the long-recognized high voltage roentgen radiation treatment have been added newer forms of destructive therapy in recent years Internal irradiation with artificially induced radioactive isotopes has proved of definite therapeutic value Radioactive phosphorus has limited application in the treatment of metastatic lesions to bone, and may produce a transitory remission in the acute leukemias and a more prolonged effect in the chronic types [10] Radioactive iodine has been used beneficially in certain malignancies of the thyroid with metastases to bone and soft tissues [11] Chemotherapeutic agents such as the nitrogen mustards,[12] urethane[13] and certain folic acid antagonists (aminopterin[14]) are currently giving promise of a more effective control of the acute leukemic states in the future Effects of urethane in controlling the clinical and hematologic phenomena in certain patients with subacute and chronic myeloid leukemia (Fig 158) have been encouraging The dosage varies from 0 3 to 5 gm daily in divided doses, administered in regular or enteric-coated capsules or in solution (1 gram per 5 cc of a vehicle as aromatic elixir) Some twenty-seven other carbamate molecules tested have failed to give comparable antileukemic control [13] When inhibition of the rapidly growing leukemic cells is effected, thus "loosening" a tightly packed cellular, relatively avascular marrow, regenerative erythropoiesis occurs promptly and spontaneously In progressive osseous and fibrous tissue replacement of normal marrow, substitution therapy with transfusions is necessary Under such circumstances, splenomegaly with compensatory hematopoiesis may reflect a reversion to the spleen's earlier embryonic function of hematopoiesis (myeloid metaplasia) Splenectomy under such circumstances, of course, is contraindicated even when there is coincidental evidence of hypersplenism

Toxic Cellular Marrow Inhibition, Destruction and Functional Impediment.—Most of those anemias, formerly considered to be the result of an "idiopathic" marrow hypoplasia or aplasia have, in recent years, been traced to specific insults to the mesenchymal erythrocyte precursors by noxious chemical, bacteriologic, chemotherapeutic or physical agents in their environment Recovery depends on the severity and duration of the toxic exposure and the inherent susceptibility or resistance of the individual's original hematopoietic endowment. Many agents, from both exogenous and endogenous sources, have been incriminated as potential erythroid depressants Industrial solvents, heavy metal drugs and radioactive materials have been the most frequently incriminated exogenous toxins In industry benzene toxicity was relatively common before adequate protection was provided for the worker (Fig 159) In medical therapy the organic arsenicals, sulfonamides, and gold compounds are among the most frequent potential bone marrow toxins encountered,

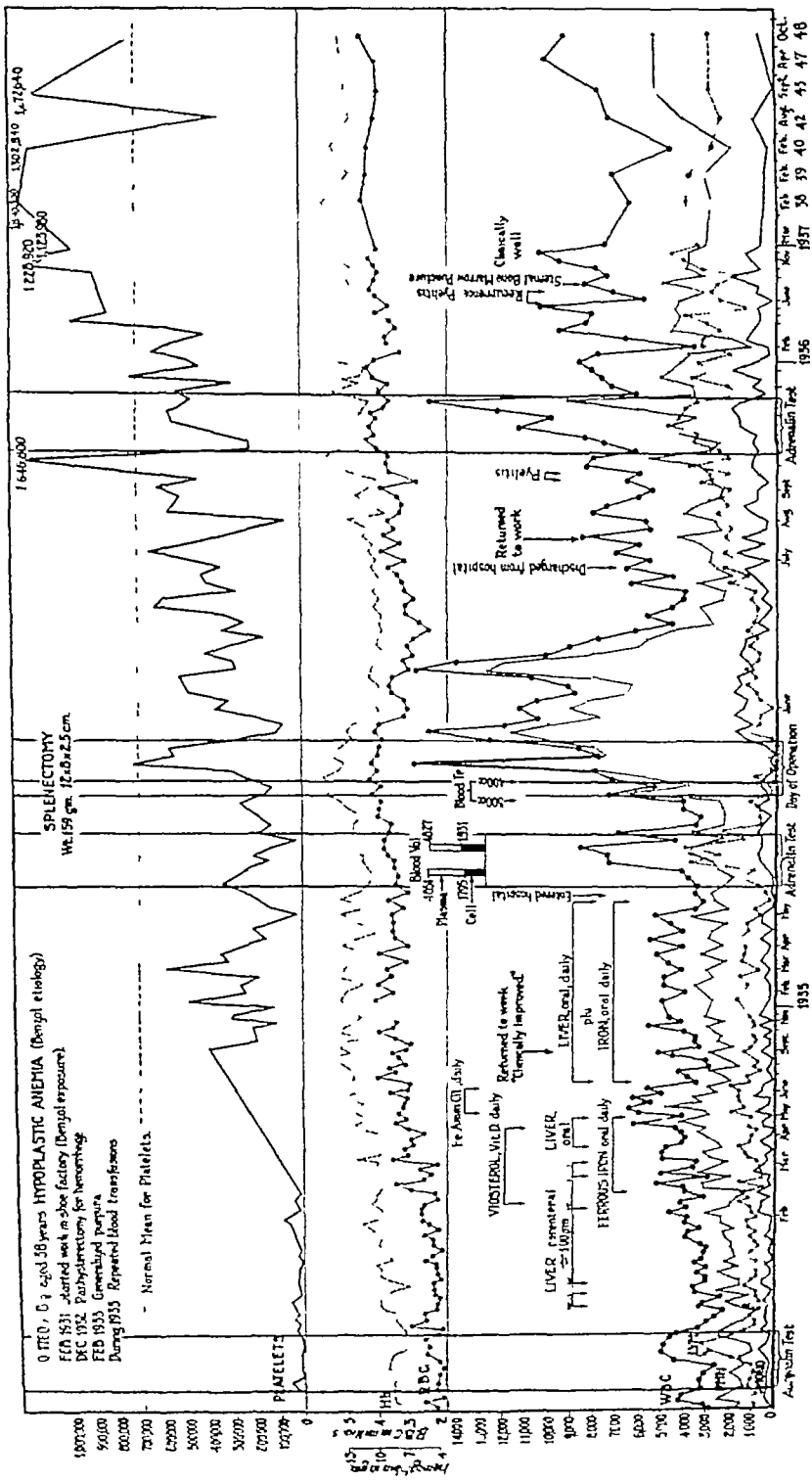

Fig 150 —True marrow hypoplasia secondary to industrial benzol exposure with recovery of badly decompensated marrow lasting 13 years Following removal from exposure and 1½ years of optimum reparative hematopoietic therapy, bone marrow had been only partially recompensated Red cells had plateaued at 3,000,000 and white cells at 3500 to 4000, the platelets were in unstable equilibrium, frequently falling below 50,000 with spontaneous petechial showers Adrenalin test revealed transitory increase in circulating elements without evidence of splenic enlargement Splenectomy was advised on basis of removing its physiologic reservoir function and at same time to release full hematopoietic function potential of marrow That one or both of these mechanisms was successfully invoked is attested by subsequent return to and maintenance of normal to high normal circulating cellular requilibration which has been maintained to the present (See also Fig 163)

and when their administration is required, constant and persistent hematologic vigilance is mandatory Erythropoietic toxicity has also been noted after the use of atabrine,[15] bismuth, mercury, colloidal silver, dinitrophenol, trinitrotoluene, certain hair dyes[16] and erythrol tetranitrate[17] An intense single dose or chronic exposure to radioactivity may produce irreversible marrow damage, as was dramatically seen in the Hiroshima and Nagasaki atom bomb explosions With the increasing availability and distribution of radioactive isotopes, the responsibility for keener alertness in the prevention as well as in the early detection of overexposure cannot be too strongly emphasized

Products of renal and hepatic insufficiency have been the most common of the endogenous toxins These toxic catabolites have mostly exerted their effect on the erythrocyte progenitors, more rarely on the maturation cycle

The primary considerations in therapy are early recognition and prompt removal of the offending contact. When it is an industrial toxin this, of course, requires removing the ill person from the noxious environment It means a search for other exposed susceptible persons and the institution of protective safeguards for all potential victims For eliminating or decreasing an endogenous toxin, one has to correct or alleviate the primary metabolic dysfunction, generally either hepatic or renal insufficiency Full advantage must be taken of reversible states, including organic recompensation and tissue repair, with the appropriate treatment. The extent of substitution transfusion therapy required will depend on the extent and permanency of the damage to the multipotential primitive connective tissue mesenchyme in the marrow When the full-blown clinical syndrome is encountered prolonged blood transfusion support should be undertaken and not discontinued even after weeks and months in some patients since bone marrow regeneration and recovery may take place only after months of latency

Other toxic agents have their effect on the later rather than the earlier phases of erythrocyte development Recent investigations on the anemias secondary to infection seem to point toward an interference with the proper utilization of iron in the formation of the hemoglobin molecule[18] Even though iron may be absorbed and stored in the iron depots, there is apparently a "block" in its adequate utilization A similar condition exists in lead poisoning, in which there is also an interference with proper hemoglobin synthesis Therapy again must be directed toward eliminating the basic cause Continuing research activity in this field gives promise of more effective control as more knowledge is obtained

Deficiency of Essential Maturation Materials.—As has been previously noted, different stimuli and materials are necessary at specific points in the erythrocyte maturation cycle for adequate development

The first of these is the so-called *erythrocyte maturation factor* (EMF), which is essential to the evolution from megaloblast to erythroblast Any deficiency in this vital factor results in a "maturation arrest" at the megaloblast levels, without, however, interference in megaloblast multiplication This abnormal hyperplasia of megaloblasts in the bone marrow is reflected in the peripheral blood by a more or less profound macrocytic anemia, neutropenic leukopenia with the nuclear hypersegmentation in those neutrophils present and thrombocytopenia

In 1929, Castle found that this erythrocyte maturation factor was deposited in all normal livers, the result of a metabolic interaction between an "extrinsic factor" supplied in the diet and an "intrinsic factor" supplied by the gastric glands [19 20] A simple but important formula was thus derived *Extrinsic Factor* (Food) + *Intrinsic Factor* (Stomach) = *Erythrocyte Maturation Factor* (Liver) Utilizing these data, it may be readily seen that a "macrocytic anemia" will result from any interference with the completion of this essential sequence of metabolic events Any inadequacy of the "extrinsic factor," which is obtained principally from eggs and meat, results in the so-called "nutritional macrocytic anemia," which has been prevalent in so many parts of the world in recent years (Fig 160) [21] A macrocytic anemia with megaloblastic arrest of the bone marrow is not uncommonly encountered in infancy and is frequently associated with a histamine-refractory achlorhydria Occasionally a specific lack of extrinsic factor, as in an infant whose diet has been principally goat's milk, can be incriminated, but in most instances whether it is a lack of either the extrinsic or intrinsic factor or both has not been satisfactorily determined These anemias will respond satisfactorily to intensive liver concentrate or to folic acid therapy

In addisonian pernicious anemia there is an inadequacy of the "intrinsic factor" supplied by the gastric mucosa Any mechanism which interferes with adequate absorption from the gastrointestinal tract as in sprue, or from any hypermotility as from surgical anastomoses or *Diphyllobothrium latum* infestation, may be reflected in the peripheral blood by a macrocytic anemia When hepatic storage of EMF is interfered with, as is occasionally seen in advanced cirrhosis, then a similar type of macrocytic anemia may develop and persist despite intensive liver extract or folic acid therapy This would suggest that the intact liver is necessary for making the EMF available to the bone marrow

Since certain extracted concentrates of liver have been the most readily available and most effective sources of EMF, the therapy of most of the macrocytic anemias has been based on the use of this material in dosages of 20 units per 1 cc , daily or at longer intervals, as determined by the

response of each individual patient Supplying the definitive erythrocyte maturation factor has been more expedient and direct than attempting to supply either extrinsic or intrinsic factors as such Maintenance dosage

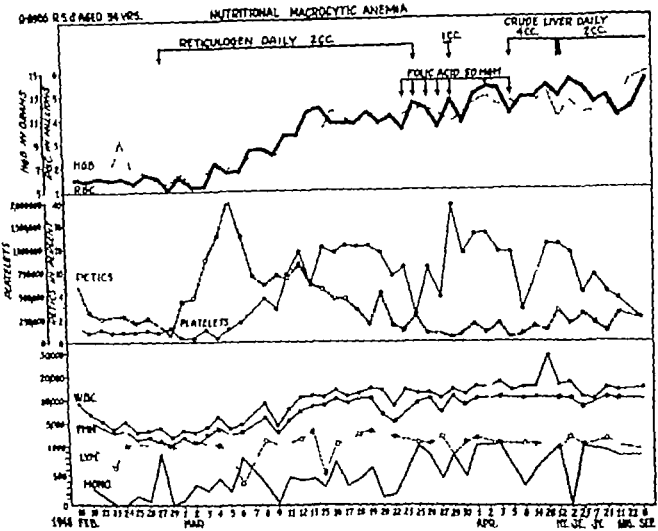

Fig 160 —Six surgical operations for tuberculous enteritis during the period 1935–1945 resulted in an extreme hypermotility of the gastrointestinal tract in this patient. To minimize the irritability the diet was strictly limited to potatoes and a little meat on rare occasions (extrinsic factor deficit) The progressive macrocytic anemia which developed over a two year period was accompanied by thrombocytopenia both of which reflected a megaloblastic hyperplasia of the bone marrow Free hydrochloric acid was present in the stomach secretions Following parenteral liver concentrate (2 cc. daily) there were excellent reticulocyte platelet and granulocyte responses The red cells and hemoglobin, however, plateaued on this regimen at approximately the 4 million level Folic acid was then administered with a further elevation of both red cells and hemoglobin Both tuberculosis and the anemia have remained under control since March 1948 with a weight gain of 25 pounds Except for a mild diarrhea resulting from the surgical detours of the intestines there are no present complaints

varies from patient to patient, and in the same patient at different times, as for example during infections

With the isolation (from liver and yeast), identification and later the synthesis of pteroylglutamic acid (folic acid), a new impetus was given to the study of the macrocytic anemias This synthetic molecule, though

not identical with the active principle in liver extract, can affect specifically the normal maturation of the megaloblast, in dosages of 2 to 10

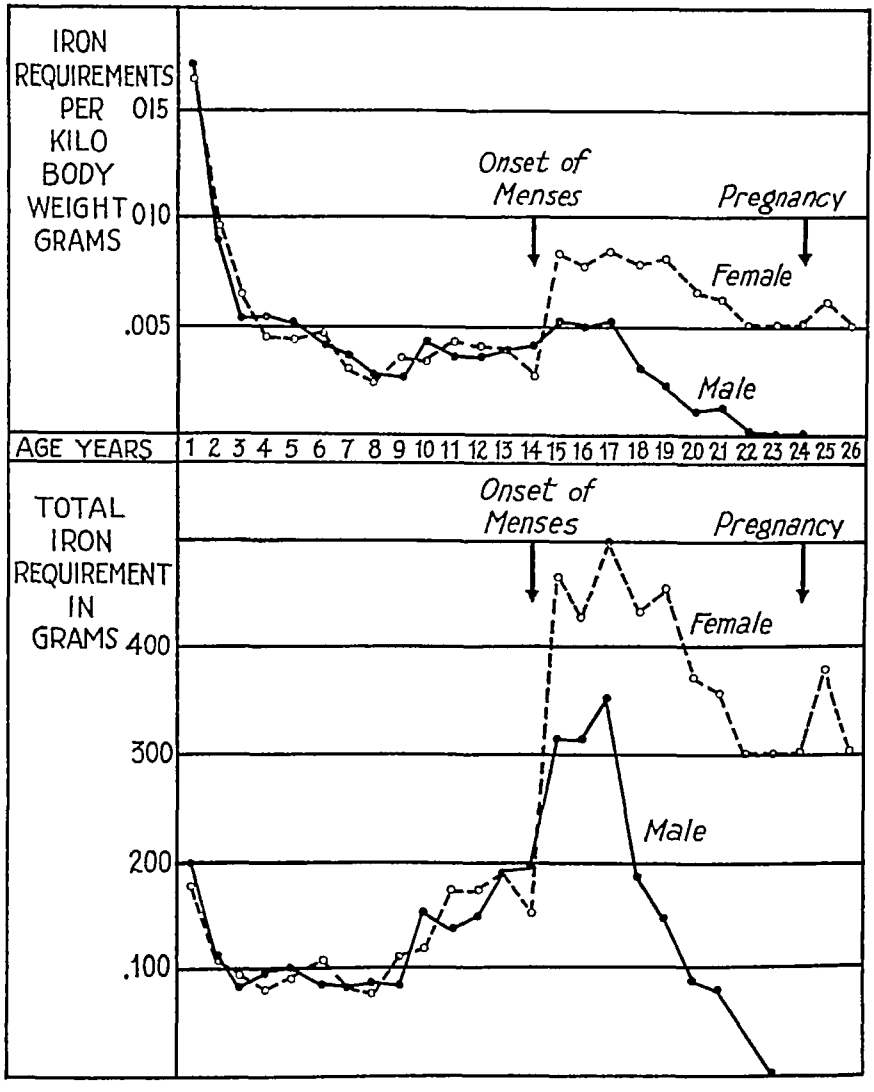

Fig 161 —The estimated iron requirements from infancy to full adulthood Note the increasing requirements which parallel growth and development in both male and female, until the onset of menses and pregnancy in the female make increased demands The dietary iron requirement in the adult male become negligible (After Heath, C W and Patek, A J , Jr Medicine, Vol 16)

mg per day, given orally or parenterally, i e it has an "erythrocyte maturation factor" effect Pteroylglutamic acid (PGA, or folic acid) has been used with complete success in correcting the hematologic aspects in most of the cases of pernicious anemia, *but it has failed effectively to control the neurologic manifestations* It is now evident that multiple

chemical complexes are present in the therapeutic concentrates of liver which together are necessary to maintain both the integrity of the central nervous system and adequate erythropoiesis

Very recently a complex organic molecule containing cobalt known as vitamin B_{12}, has been isolated from liver, and in the preliminary clinical tests it has been reported as proving exceptionally effective in promoting megaloblastic maturation in pernicious anemia [2 3] As little as 0 75 microgram daily has been found to produce a maximum reticulocyte response with subsequent red blood cell and hemoglobin increases There has been insufficient time to establish its effectiveness in permanently controlling the neurologic manifestations as well, however, the early reports are favorable [22]

Proteins play a major role in the synthesis of hemoglobin and apparently this function has biologic priority on both currently administered and stored, reserve protein [5] Recent work indicates that the amino acid glycine is essential for protoporphyrin synthesis [6] Iron combines with the protoporphyrin ring to form the heme molecule Heme plus globin, a protein similar to albumin, completes the hemoglobin molecule

An inadequate supply of iron for this synthesis results in hypochromic anemia Chronic blood loss with insufficient dietary replacements of the lost iron is the most common cause of this type of anemia and is most frequently seen in women during their active menstrual life (Fig 161) Iron reserves in men are conserved with exceptional efficiency, and when an iron deficiency (hypochromic microcytic) anemia is exhibited in man, a thorough search for some occult source of blood loss must be made Frequently, this type of anemia is the earliest and only sign of a peptic ulcer or malignant growth of the gastrointestinal or genitourinary tract [22]

In man the ferrous salts (optimum oral dosage 0.3 gm t i d) are more efficiently absorbed than the ferric salts (optimum oral dosage 1 gm t i d) [24] Ferrous gluconate appears to be less irritating to the gastrointestinal tract than many of the other available iron salts Intravenous iron therapy is both unnecessary and dangerous [25]

Anemia is a frequent accompaniment of hypothyroidism A tendency to macrocytosis is common and the bone marrow usually shows a moderate shift to the left to the erythroblast stage Corrective thyroid therapy is specific for the anemia, as the basal metabolic rate is brought to normal

ANEMIAS DUE TO EXCESSIVE PERIPHERAL DEMAND (LOSS OR DESTRUCTION)

Clinical anemia in the presence of an hyperactive marrow for erythropoiesis focuses one's attention at once on some peripheral mechanism as the causative factor Excessive peripheral destruction of erythrocytes is

usually reflected in the blood by a microcytic anemia, reticulocytosis and elevation of the protein-bound serum bilirubin (indirect Van den-Bergh) The destruction may occur either intravascularly or extravascularly

Intravascular destruction may be due to circulating hemolysins and/or agglutinins, to an inherent cellular defect, as in sickle cell and Mediterranean anemias, to infections, particularly malaria, or infections caused by bartonellae or hemolytic streptococci, to other poorly understood etiologic agents grouped under the general diagnostic category of acquired hemolytic anemia If a specific hemolytic agent can be identified, then treatment is centered on removal of this cause, for example, elimination or control of a hemolytic infection, the removal of a patient from the exposure to industrial toxins, the prevention of exposure to cold in paroxysmal cold hemoglobinuria, or the institution of an exsanguination replacement blood transfusion regimen in erythroblastosis fetalis The success of such treatment must always depend on the accuracy of the determination of the cause In the so-called acquired hemolytic anemias in which a specific antigen cannot be determined, splenectomy has proved effective in approximately 60 per cent of the cases [26] This strongly suggests a high degree of localization or concentration of the hemolytic activity in the parenchyma of the spleen, a well demonstrated reservoir for normal red blood cells, with a corresponding accentuation of cellular sequestration under a variety of pathologic conditions

The spleen is the principal organ for clearing the blood stream of debris, including damaged, sensitized, debilitated and senile blood elements The splenic circulation is ideal for the physiologic stagnation of the blood stream, with a corresponding sequestration and concentration of the formed elements as the plasma continues its circulation The splenic sequestration of the blood cell elements brings them in close and prolonged contact with the large number of reticuloendothelial clasmatocytes normally present, thus favoring phagocytosis of the physiologically senile elements King pointed out, as early as 1914, that it would be quite possible for this "normal mechanism" to become accentuated pathologically, should the spleen, for any reason, fail to discriminate between senile and normal cells [27] For this hypothetical condition he proposed the term "hypersplenism " Since that time, and more particularly during the past ten years, clinical evidence has accumulated which strongly supports this hypothesis

The beneficial effect of splenectomy in congenital hemolytic icterus has been recognized for many years The marrow in such patients is found to show marked normoblastic hyperplasia consistently With the surgical removal of all splenic tissue, effective "cure" can be accomplished in approximately 98 per cent of the cases This so-called "trait",

which is characterized by spherocytic erythrocytes, is inherited as a *mendelian dominant gene factor and may be manifested clinically in any* degree from a chronic undermining and frequently debilitating anemia to the dramatic, acute, fulminating hemolytic crisis (Fig 102) The

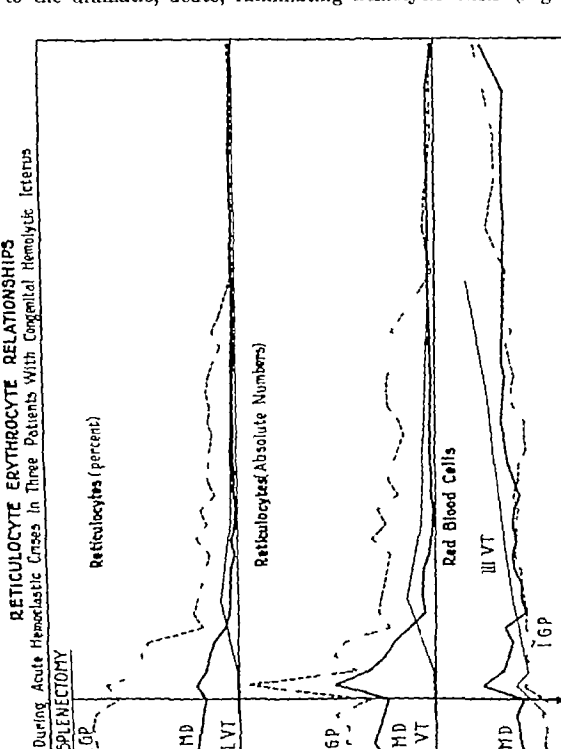

Fig 102 —Three hemolastic crises in patients with congenital hemolytic icterus are contrasted as to respective preplenectomy reticulocyte levels to determine if postplenectomy erythrocyte recovery may be predicted therefrom Patient III, with lowest number of circulating platelets, showed most rapid return of circulating red blood cells to normal though recovery was prompt and complete in all three cases.

former may be precipitated into the latter by a number of physiologic or pathologic factors which may modify the usual homeostatic equilibrium of the individual, such as pregnancy, bone fracture or mild respiratory infection In acute crisis, preoperative transfusions are not indicated, regardless of the depressed red blood cell level, in that as soon

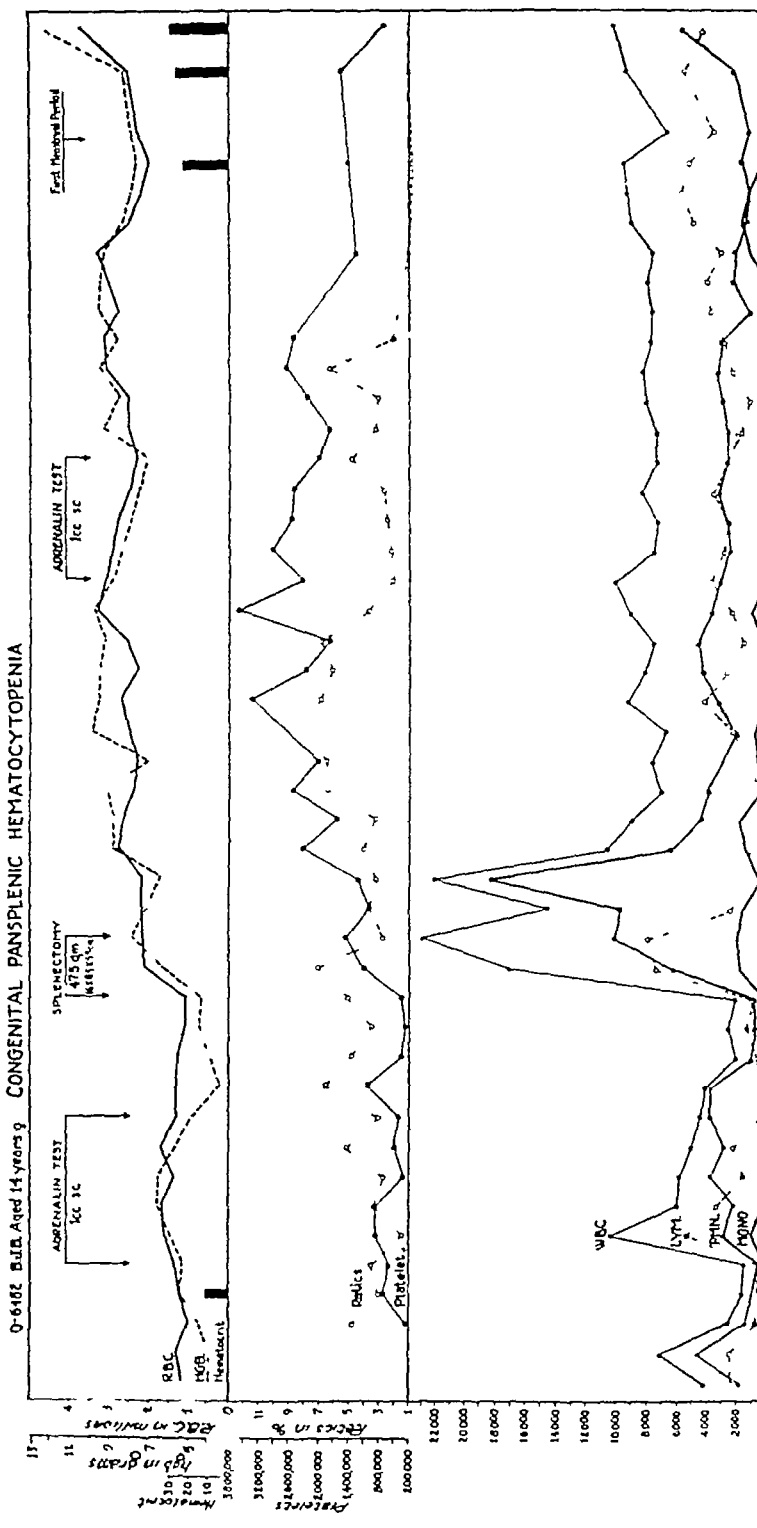

Fig 163 —This 14 year old girl, severely pancytopenic with profound anemia, thrombocytopenia and neutropenic leukopenia from infancy, had been given a diagnosis of aplastic anemia Appropriate studies, however, revealed a panhyperplasia of qualitatively normal marrow elements, and an adrenalin test reflected splenic hypersequestration of all circulating blood cells Splenectomy was immediately followed by the successful establishment for the first time in her life of a normal cellular equilibrium for all the peripheral blood elements A chronic invalid has become a normal young woman This dramatic response continues to be sustained without other therapy to the present, 5 years after splenectomy Compare this true primary hypersplenism with the toxic hypoplastic anemia with a relative physiologic hypersplenism charted in Fig 159

as the surgeon is able to visualize the spleen, injection of adrenalin into the pulp and manual manipulation will autotransfuse as many as 2 million per cubic centimeter of sequestered red blood cells (350 to 500 cc packed red cell volume) into the general circulation via the splenic vein before the splenic pedicle is clamped and the spleen removed [28] Actually, preoperative transfusion is contraindicated in that it frequently appears to add fuel to an already extensive conflagration of cellular destruction

It has long been argued whether this cellular defect of spherocytosis is of central (bone marrow)[29] or peripheral (spleen) origin,[30] i e whether the spherocytosis is a manifestation of an inherited defect in cell production or the result of exposure to an inherent hemolysin or hemagglutinin making splenic sequestration and phagocytosis the ultimate or basic pathologic mechanism Evidence is accumulating to support the concept of an unstable immunocatalytic mechanism as playing a significant role in the basic etiology These studies are at present of more theoretical than practical interest and have no direct bearing on the proved efficiency of and necessity for therapeutic splenectomy in these patients

Congenital hemolytic icterus is only one of several primary hypersplenic syndromes Primary splenic neutropenia involves not only an extremely low circulating neutrophil level, but the bone marrow must show specific hyperplasia of the neutrophilic myelocytes without maturation arrest or evidence of toxic damage [31] Splenic thrombocytopenic purpura reveals a marrow hyperplastic for megakaryocytes but with few or no platelets in the peripheral circulation [32] Splenic panhematopenia involves a paucity of all of the circulating blood elements, but with the bone marrow showing extreme overcompensatory pan-marrow hyperplasia, all cell types being fundamentally normal[33] (Fig 163)

When the spleen is removed in such syndromes there is an immediate alleviation of the specific cytopenia Examination of the splenic parenchyma immediately after removal, with the living cell supravital technic, reveals numerous phagocytic clasmatocytes (macrophages) which have engulfed and begun digestion of the specific element and/or elements involved in the peripheral cytopenia No pathology other than cellular hypersequestration and hyperphagocytosis is demonstrable in the surgically removed splenic tissue in the primary type of hypersplenic syndrome

It has been recognized, relatively recently, that in those general systemic diseases secondarily involving the spleen, hematologic syndromes clinically indistinguishable from the primary types of hypersplenism may occasionally be precipitated [34] In these instances, as in the primary syndromes, attempts at specific cellular compensation in the marrow may be recognized (Fig 164) At such times the cellular deficiency in the blood may be the chief threat to life and splenectomy

may be a lifesaving measure Such primary diseases as Boeck's sarcoid, Hodgkin's syndrome and chronic leukemia may even be more effectively treated after the removal of an extensively involved spleen

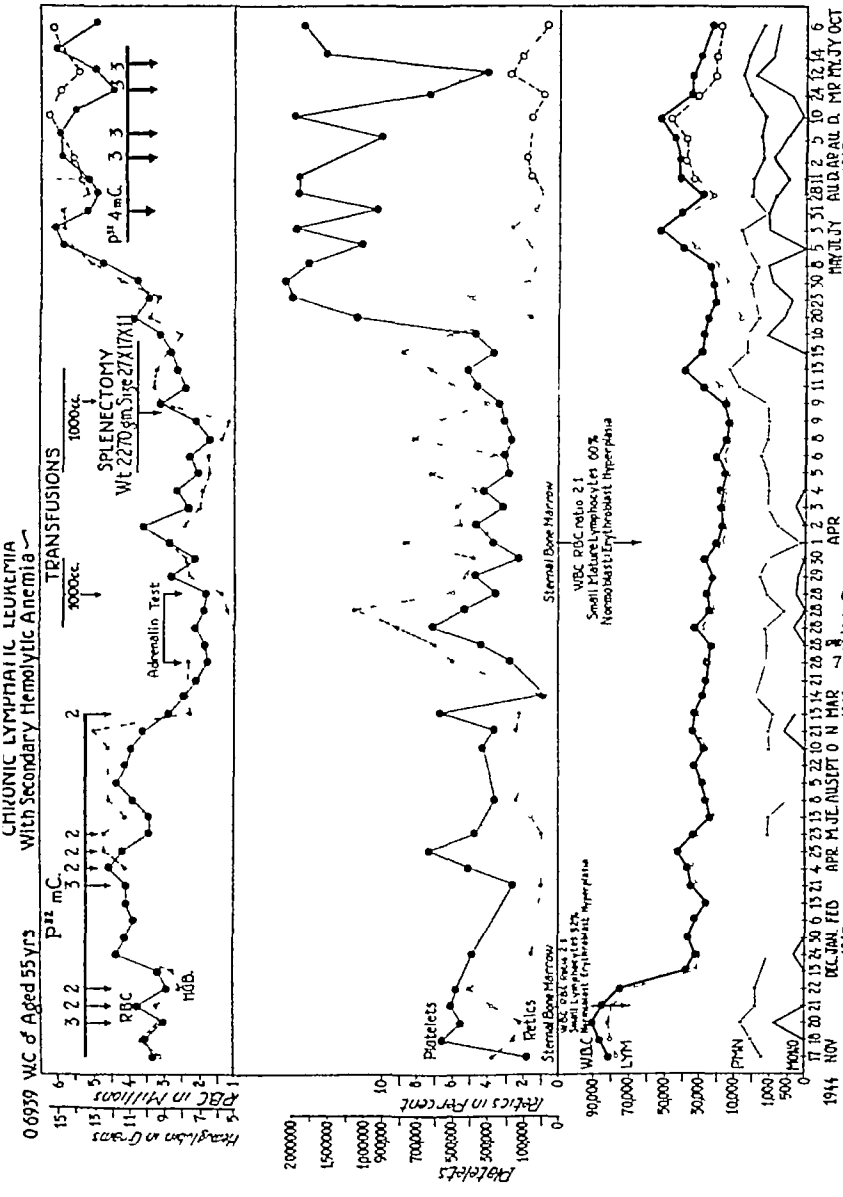

Fig 164 —After 1½ years of successful control of chronic lymphatic leukemia with radioactive phosphorus, spleen enlarged rapidly and acute hemolytic anemia with jaundice developed, with no other clinical or hematologic evidence of an exacerbation of the leukemic process Bone marrow showed normoblastic hyperplasia without excessive lymphocytic infiltration No family history of congenital hemolytic icterus Secondary hypersplenism was diagnosed Splenectomy was followed by a remission maintained to present—2½ years after operation No tendency to recurrent hemolytic anemia has been noted Small intermittent dosage of radioactive phosphorus controls the leukemic process now for the fourth year

The diagnosis of the hypersplenic states is made on (1) the history, (2) physical examination, (3) peripheral blood examination, (4) bone marrow examination, and (5) the adrenalin test The history may be that of an acute fulminating hemolytic crisis or of a long-standing chronic mild anemia with or without jaundice The physical examination

usually reveals a clinically enlarged spleen, but this is not necessarily true in every instance The spleen may be significantly enlarged without being demonstrable by examination Peripheral blood studies reveal varying degrees of anemia, with or without spherocytosis, elevation in the reticulocytes, reflecting the bone marrow's attempt to compensate for the peripheral destruction, elevated indirect Van denBergh reaction and increase in the osmotic fragility of the red blood cells The urobilinogen excretion in the urine and feces is increased Bone marrow examination reveals compensatory hyperplasia of the erythrocytic elements to a degree which is directly proportional to the extent of the peripheral destruction as well as to its own ability to respond to the increased demands Hypersequestration of the red blood cells in the splenic parenchyma can be demonstrated by the adrenalin test, which causes contraction of the smooth muscle of the spleen with ejection of the sequestered erythrocytes into the general circulation

An absolute diagnosis of the primary form of hypersplenism involving the red blood cells, i e congenital hemolytic icterus, is made only by demonstrating the spherocytic trait in other members of the patient's family, as spherocytosis and increased osmotic fragility are not confined to the congenital type alone

Post-Splenectomy Relapses.—Recurrences of the hemolytic anemia after splenectomy may be due to one of two mechanisms (1) Accessory splenic tissue, which is found in approximately 35 per cent of all persons,[12] may hypertrophy and precipitate episodes similar to the primary syndrome (Fig 165) Thus, it is extremely important that accessory spleens be looked for and removed at the time of the original splenectomy (2) Very rarely a generalized reticuloendothelial cell hyperphagocytosis occurs, so that removal of the large splenic focus fails to correct the clinical syndrome permanently In these very infrequent instances, excessive erythrophagocytosis and destruction may be seen in the Kupffer cells of the liver and in the clasmatocytes of lymph nodes, bone marrow and lungs This condition has been designated *generalized reticuloendothelial cell hyperphagocytosis*

A sine qua non for the diagnosis of "hypersplenism" is a compensatory hyperplasia in the marrow of the specific cell types which are deficient in the blood Splenomegaly per se is not an indication for splenectomy Occasionally the splenomegaly may reflect active hematopoiesis as a compensatory response to inadequate cell production in the bone marrow, an embryonic reversion by which it may become the body's most important site of blood cell formation When the bone marrow is replaced by fibrous or osseous tissue splenectomy is *of course, contraindicated*

Anemias of chronic blood loss are doubly represented in this classification, in that they are iron deficiency anemias and as such have been

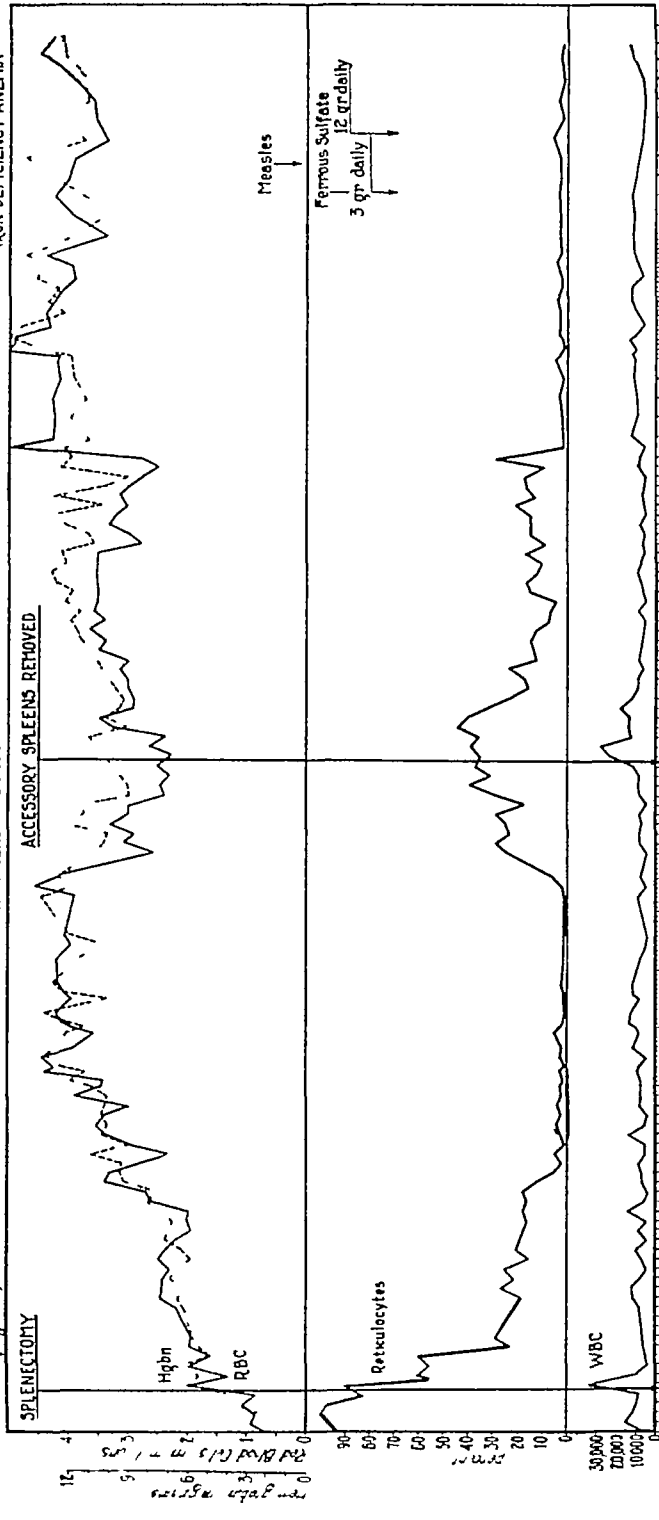

Fig 165 —An acute hemoclastic crisis was terminated by emergency splenectomy in this patient at the age of 4 years A prompt and complete remission continued for four years and four months, at which time the hemolytic jaundice recurred Re-exploration revealed three small accessory spleens at the site of the original ligation of the splenic pedicle Their removal was followed by an hematologic and clinical remission lasting to the present time ten years since the second operation, fifteen years since the original splenectomy Liver and lymph node biopsies failed to reveal any reticulo endothelium cell hyperplasia or hyperphagocytosis such as were present in spleen and accessory spleens in this patient

considered in the discussion of anemias of central bone marrow origin

SUMMARY

Anemia is an imbalance between erythrocyte production in the bone marrow on the one hand and peripheral erythrocyte destruction or loss on the other

Inadequate or defective erythrocyte production may be caused by (1) an inherent genetic defect, (2) a mechanical replacement (myelophthisis) of normal erythrocytic elements by malignant metastases to the marrow, or by leukemic, fibrous or osseous marrow replacement, (3) toxic cellular inhibition, destruction and functional hypoplasia, and (4) deficiency of essential materials necessary for adequate maturation

Excessive peripheral demand may be seen in the various primary and secondary hemolytic anemias and in blood loss Failure of the full bone marrow potential for erythropoiesis to compensate for the increased peripheral dissolution results in anemia

Only in the determination of the specific defect or defects can intelligent and successful therapy be accomplished *Specific therapy demands precise diagnosis*

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DIETARY NEEDS IN LONG-TERM ILLNESS

JAMES S McLESTER, M.D., LL.D., F.A.C.P.*

A PERSON can be cured of scarcely anything by starvation. To overcome the debilitating effects of illness he needs food. True, the formation of malignant tumors in experimental animals has been retarded by the rigid restriction of caloric intake, and the resistance of mice to the virus of poliomyelitis is said to be increased by thiamine deficiency, but, interesting as these experiments are, there is no evidence that they can be applied directly to man. Clinical experience tells convincingly of the need for adequate food in the prevention and treatment of disease. This is especially true of long-term illness.

The day was when, in the effort properly to nourish his patient, the physician told him what he must not eat. Today he tells him what he must eat. This about-face took place about forty years ago when it was found that two diseases, typhoid fever and peptic ulcer, could be more effectively treated with diets that were vastly more liberal than those then in vogue. The fear of injuring the ulcer, whether of the ileum or of the stomach, was discarded and diets were adopted which more nearly approached the patient's nutritive needs. The results were graphic, especially in typhoid fever, and a new era was introduced in the dietary treatment of disease.

If his illness is brief the patient can withstand the effects of enforced starvation, but not so if it is a long-term illness. In the latter, if he is eventually to regain his vigor, he must be adequately nourished. In the effort to accomplish this it is seldom necessary to emphasize the need for any one group of foods, for as a rule the nutritive requirements of the patient with a long term illness differ but little from those of the well person. The chief effort should be, in spite of the handicaps imposed by the disease, to meet normal requirements.

BASIC DIETARY REQUIREMENTS

Protein requires greatest consideration. This is becoming increasingly evident in the need for this foodstuff exhibited by patients with chronic infections, for animal experiments would indicate that there is a direct relationship between the amount of protein consumed and the efficiency of both phagocytic activity and antibody formation. In health it is assumed that it is sufficient if protein supplies 15 per cent of the caloric

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value of the diet and this applies also in most forms of chronic illness Occasionally, however, as occurs after surgical operations, burns and many other forms of acute trauma, the protein losses are enormous and these must be made good Even bed sores are more frequent in patients whose plasma protein content has been permitted to fall to a low level It would appear, then, that expeditious convalescence often depends in no small degree upon the adequacy of the protein intake

Carbohydrate is ordinarily looked upon solely as a source of energy, but it should be emphasized that it is also essential to the proper utilization of the other foodstuffs For economy in nutrition it should supply at least 50 per cent of the calories of the diet This applies in illness as well as in health The need for *fat* is seldom pressing, for the average diet will as a rule carry sufficient fatty substances to meet requirements for the essential fatty acids In the arrangement of the diet, therefore, fats need be provided only in amounts sufficient to promote normal intestinal function and to bring caloric values to the proper figure

It is necessary always to give some thought to the supply of *vitamins* and *minerals*, for chronic illness often imposes an increased burden not only on the patient's metabolism but also a serious handicap upon his ability to digest and utilize many nutritive substances Omitting from consideration the needs of the patient with frank deficiency disease, it can be assumed that the well balanced diet which includes milk, eggs, meat, green vegetables and citrus fruits (or tomato juice) will as a rule supply all needed vitamins This does not apply, however, if the diet is restricted, as in peptic ulcer or irritable colon, or if the metabolism is increased, as in hyperthyroidism and in febrile diseases In such cases additional vitamins, notably those of the B complex, should be supplied in concentrated form Brewers' yeast is a good source of these factors as well as an excellent source of protein, but its usefulness is limited by its bad taste and because it is sometimes not well tolerated I know of nothing better for this purpose than intragluteal injections given once or twice weekly of a solution of crude liver extract (3 cc), to which thiamine (50 mg) has been added The crude extract (not the highly refined product!) supplies many essential substances, some of them known and some unknown, and therefore is often a useful adjunct to the regimen of chronic illness

For mineral supplementation, the most frequently needed elements are calcium and iron If the patient cannot or will not take milk and if because of intestinal difficulties he must avoid the leafy vegetables, then he should be given calcium The iron deficiency anemia, which accompanies many forms of chronic illness, especially when there is loss of blood, requires the administration of iron There are many hazards to the absorption and utilization of this element, however, and it is often advisable to prescribe it in liberal amounts

SENILITY

The most common long term illness is senility It is accompanied by many disabilities, notably of the digestive tract Witness the achlorhydria of a great many elderly people Because of the restriction placed on his activities the old person obviously does not require as much food as the vigorous young man, but to permit him markedly to curtail his food, as is often done, is a mistake As one writer aptly puts it, "the tea and toast regimen for Grandma is out " She needs real food to maintain adequate nutrition

The lack of appetite that comes at this time applies particularly to meat, but to permit the old person to omit meat entirely is a mistake He should take each day at least one helping of meat, fish or fowl, also one or two eggs In old age, as in childhood, milk is a highly desirable food, say, three glasses daily Equally pressing perhaps, is the need for fruit, particularly of the citrus variety, and for green vegetables The latter in extreme old age may be taken in pureed form Other foods should be eaten in amounts sufficient to give to the diet a calorie value of about 2000 calories, often more

CHRONIC TUBERCULOSIS

The dietary needs of chronic tuberculosis have always been given great consideration but in times past the mistake was made of trying to fatten the patient Forced feeding was often the rule, and marked gain in weight even to the point of obesity was looked on as a most satisfactory sign This is an error Gain in weight follows improvement, but improvement does not necessarily follow forced gain in weight It is an obvious error always to regard obesity as an evidence of robust health It is coming to be more and more realized that, other things being equal in health or in disease the lean person is the more robust and that he has the greater life expectancy Scrutiny of patients who have recovered from tuberculosis and who have long remained well is proof of the truth of this, they are seldom fat The tuberculous patient should be well nourished and should maintain his body weight at a figure which is equal to or perhaps a few pounds above the calculated ideal but he should not become fat

The diet should be adequate The patient with pulmonary tuberculosis of moderate grade with little or no fever requires about the same food, in slightly increased amounts, as in health A man weighing 70 kg who is up and about but is doing no work will need 40 to 45 calories per kilogram of body weight, approximately 2800 to 3000 calories If he is working at some light occupation this should be increased to 200 or 300 calories Protein should be permitted in liberal though not excessive amounts for the average patient from 100 to 150 gm daily The

belief of the older clinicians in the value of a generous fat diet in tuberculosis is borne out by the observations of McCann that fat, in contradistinction to carbohydrate, increases the respiratory volume but little Carbohydrate, however, should furnish at least 50 per cent of the energy The diet should supply also an abundance of vitamins and minerals For women these figures may be decreased about 8 or 10 per cent The younger the patient, the greater the proportionate caloric need and protein requirement These figures are merely tentative, for experience has demonstrated the existence of great differences in the food requirement of individual patients The physician should use good judgment and should be guided somewhat by the patient's appearance, vigor and sense of well-being

CHRONIC HEART DISEASE

Chronic cardiac disease, with or without myocardial failure, demands a moderately subcaloric ration If the heart is still competent though failure is threatened, the regimen should be such as will reduce the body weight to 10 to 15 per cent below the calculated normal and will depress the basal metabolism in like degree This diet should be (*a*) relatively low in caloric value, (*b*) somewhat restricted in protein, (*c*) fairly high in carbohydrate and (*d*) low in salt In the beginning the caloric value of the diet may be as low as 1000 calories with perhaps 60 gm of protein This should not, however, be continued long as it may lower cardiac efficiency After the weight has been effectively reduced and the metabolism lowered, these values may be raised to 1800 to 2000 calories with 70 gm of protein A little later the total value of the diet should be increased to a maintenance figure

When cardiac failure has supervened and especially when edema is present, a low sodium diet should be given, that is, one which includes no salt or salty food and in which no salt is added to the food in its preparation Unsalted butter and bread made without salt should be used Such a diet contains between 1 5 and 2 gm of sodium chloride This regimen, according to White and his associates,[1] should provide 1800 to 2000 calories and should contain about 70 gm of protein Fluids should be permitted freely, up to 2 to 3 liters in the twenty-four hours The authors just quoted report excellent results from this diet in the treatment of congestive heart failure Sodium restriction, however, is not entirely without its dangers Vague weakness with diarrhea may occur elevation of blood urea with uremia has been reported[2] The possibility of such untoward effects should be kept in mind

The same principles are applied in the "Karell milk cure," an undernutrition diet devised for patients with congestive heart failure This regimen permits during the first four or five days four glasses of milk

(800 cc.) in the twenty-four hours and no other food, little additional fluid is given. Later, the amount of milk is increased to 1000 cc. and other simple foods such as soft boiled eggs, cereals with cream, toast with unsalted butter and preserves are added. This regimen is not used as much as formerly but it is still sometimes prescribed with satisfactory results.

CHRONIC KIDNEY DISEASE

Latent Glomerular Nephritis.—The patient with chronic nephritis has been subjected in years past to great dietary restriction, much of which, notably in respect to protein, was unnecessarily rigid and probably harmful. Following the acute stage of glomerular nephritis there may come a latent period lasting many years, during which time the patient should enjoy a diet that is calculated to maintain his nutritive state at the highest possible level. If the protein losses of the acute stage are still felt, as may be evident in a low level of plasma proteins, then the protein quota of his diet should be liberal, as much say as 100 gm., 125 gm. or even 140 gm. daily. Later the protein allowance should be of the order of 1 gm. per kilogram of body weight, slightly more in the case of children. In other respects the diet for this latent period of glomerular nephritis should be such as will approximate but never exceed the accepted maintenance figure. Because of the handicap under which the person is laboring, some thought should be given to the vitamin and mineral content of the diet and to all other factors that will contribute to the maintenance of bodily vigor.

Degenerative Bright's Disease.—Degenerative Bright's disease requires a diet that has as its object not only the protection of the kidney but also and primarily the replacement of the protein lost in the urine. This demands, as the latent or chronic stage of the disease is approached, a liberal allowance of protein and restriction of the intake of salt. Keith and his co-workers at the Mayo Clinic emphasize the necessity during the early stages for control of both the water content and the mineral quota of the food. They found that the foods provided in their routine salt poor diets contained too much water (from 1200 to 1400 cc.) since this amount when added to that taken as fluid brought the actual daily intake of fluids up to 1800 to 2400 cc. In constructing their diet the effort was (1) to decrease the water contained, (2) to reduce the amount of sodium and (3) to control the diet so that this minimal content of water would for practical purposes be the same from day to day.

During the first two or three weeks the patient should be given a diet sufficient to meet his basal metabolic requirements, that is, one providing 1500 to 1800 calories but only 50 to 60 gm. of protein. He should take 600 gm. of fruits and vegetables, of which at least 400 gm. should be in the form of fresh fruits and green vegetables. Oranges, grapefruit,

bananas, lettuce, tomatoes and string beans are suitable Canned tomatoes and canned string beans of any standard brand may be used A liter of fluid should be permitted, perhaps a little more Certainly during the summer months and in warm climates larger amounts are needed Later, the caloric value of the diet should be increased to keep pace with the patient's increased activities The protein quota should be increased to 80 to 100 gm daily, more if the losses in the urine are great No salt should be added to the food after it comes to the table

Nephrosclerosis—In nephrosclerosis the diet should be balanced and not unduly restricted The caloric intake should be reasonably small but nonetheless sufficient to meet the patient's needs Roughly, the patient of sedentary habits can usually get along on 2500 calories daily If he plays nine holes of golf twice weekly or takes a short walk daily, he should be allowed 2800 or 3000 calories His requirements are approximately those of the normal man The obese patient should be encouraged to lose weight gradually, at the rate of from 3 to 5 pounds each month, until the ideal is reached Such reduction in weight not only conserves metabolism but lessens the burden on the heart The thin person's weight and vigor should be carefully maintained by an appropriately liberal diet

The allowance of protein should be sufficient not only to meet the patient's minimal needs but also to maintain him in the highest degree of strength and vigor for the greatest number of years In cases of mild nephrosclerosis with little or no impairment of renal function, a daily intake of 75 to 100 gm of protein is proper, and in cases of moderately severe involvement, an intake of 50 to 60 gm is adequate This permits in mild nephrosclerosis three glasses of milk daily, two eggs and one average helping of meat, in moderately advanced nephrosclerosis, three glasses of milk and one egg daily and an average helping of meat or fish three times weekly In the cases of grave involvement, the blood urea content being high and signs of impending disaster becoming manifest, the daily intake of protein should be limited to 35 or 40 gm

ESSENTIAL HYPERTENSION

The long-term illness that has been most assiduously subjected to dietary treatment is essential hypertension A host of regimens for the cure or amelioration of this disease, each including some form of dietary restriction, have been tried but none of these has been shown to be specific Each has been based on the assumption that one or another element of the diet is harmful to the hypertensive patient and therefore accelerates the disease process In no instance, however, has the truth of this assumption been satisfactorily demonstrated It is necessary to recognize two facts First, that the cause of this disease is unknown—

some of its late effects are well understood, but treatment addressed merely to these effects probably does no lasting good, and second, that this is a disease not of months or of years, but of decades and that a diet that fails for long periods to meet the patient's nutritive needs will probably hasten disaster

The most widely heralded of these regimens demands *rigid sodium restriction*[2] It is assumed by proponents of this diet that the adrenal cortex is involved in the genesis of hypertension and that there results a disturbance in sodium metabolism, but the evidence is not convincing In arranging the diet all foods, even bread and butter, are prepared without salt, no salt is added after the food comes to the table and no food which contains appreciable amounts of sodium is permitted Even fresh milk is prohibited and to permit the patient the benefits of this valuable food a sodium free milk powder has been placed on the market It is said that halfway measures will not suffice, that a diet that is merely "salt poor" is of no value The food must contain less than 0 2 gm daily of sodium

As a result of this regimen an occasional lowering of blood pressure is observed, but the significance of this is open to question That it signifies an amelioration of the underlying process has not been shown, it is yet to be demonstrated that rigid sodium restriction exerts a controlling influence on the natural history of this disease

TO AVOID IN THE "SODIUM FREE" DIET

The salt restriction must be drastic Moderate restriction is of no value

All foods, including bread must be prepared without the addition of salt, sweet or unsalted butter must be used No salty foods and no foods rich in sodium should be eaten The following foods should be avoided

Bacon	Chard
Ham	Cheese
Pretzels	Dandelion
Beer	Buckwheat
Milk	Kidney
Salted butter	Onion
Preserved meats	Oysters
Salted nuts	Haddock
Excessive amount of salted bread	Graham crackers
Olives	Canned soups
Pickles	Canned vegetables
Avocado	Sea food, all kinds
Barley	Dry cereals unless especially processed
Beans—Lima	Salad dressings
Beets	Relishes
Celery	

Drugs that contain sodium such as bicarbonate of soda and sodium phosphate should be avoided

The insipid taste of the salt-free food can be overcome by the use of specially prepared mixtures that contain no sodium This may be sprinkled on the food as desired A dash of garlic or paprica is also helpful The sodium-free skim milk powder now on the market may be used

The same generalizations apply to the *rice diet* advocated by Kempner [4] This diet was devised on the assumption that, as a result of disturbances in the metabolism of the kidney (not necessarily the excretory function), abnormal substances appear and play a role directly or indirectly in the development of hypertension and such associated phenomena as retinopathy, encephalopathy, heart disease and additional kidney disease This diet permits only 300 gm of boiled rice with sugar and fruit juices One liter of fluid is allowed Vitamins are added It provides 20 gm of protein and 0 15 gm of sodium, and its total value is 2000 calories Such drops in blood pressure as occur are generally credited to the low sodium intake rather than to the extremely low protein quota of the diet The former has just been discussed Opinions differ, and the good results reported by Kempner await further confirmation There may be harmful effects [2]

Starvation or semistarvation, without particular reference to protein, sodium or any other single element of the diet, will as a rule bring a reduction in blood pressure This applies to normal persons as well as to those with hypertension and particularly to the obese The effects of a low caloric intake has recently been described by Brozek and his associates[5] in reporting their experiments upon a group of healthy young men, and it is noteworthy that these observers sometimes saw serious untoward effects After the subcalorie regimen, following the twelfth week of rehabilitation when a large increase in caloric intake was permitted, a rise in blood pressure slightly above control values was frequent These physicians were led to the conclusion that a decidedly increased food intake following a period of semistarvation, with accompanying increase in body weight and rise in metabolism, places undue strain on the cardiovascular mechanism One of the subjects was brought by this means to the verge of congestive heart failure From their studies and from reports of other investigators, these observers conclude that the decline in blood pressure that accompanies semistarvation in normal young men is a reversible process and that when nutritive equilibrium is reestablished the pressure not only returns to normal, but may at times overshoot the mark to frankly hypertensive values

In confirmation of this, these physicians quoted reports of similar observations made in Leningrad During the two years following the famine of the war period hypertension in that city became a serious problem The number of hospital admissions for this disease in 1943 was

five times that of 1940. During the period of recovery from semistarvation not only was there a greatly increased incidence of hypertension, but there were indications that the disease existed in a severer form than previously. Retinal changes and cardiac insufficiency were much more common. It appeared that hypertension had became more frequent and of a more malignant character.

It is accepted that rigid limitation of the calorie intake will often bring a fall in blood pressure in hypertensive patients, but it is not yet proved that this fall is accompanied by a favorable change in the underlying disease process. Also, from the reports just quoted it would appear that, if the hypertensive patient adopts a semistarvation regimen, he may later, when dietary restrictions are abandoned, find himself in a more grievous state than before treatment was instituted. All of this should give the physician pause when he contemplates placing his patient upon the sodium free diet, the rice cure, or any other regimen of rigid dietary restriction. With due consideration of the hazards involved however the low sodium diet or the "rice cure" may justifiably be given a trial in cases of severe hypertension, particularly of the malignant form, provided the patient is prepared to live by the rule and understands the dangers of the treatment. The cases should be carefully selected and, for reasons just discussed, there should be no sudden return to an abundant diet or other abrupt changes in the regimen.

For the hypertensive patient whose extremity is less desperate, particularly if he is overweight, a mild reduction regimen is best. The person whose weight is normal should gradually be reduced some 10 per cent, the obese person to a figure which approximates, but not necessarily equals, his ideal weight. This diet should be moderately subcaloric but balanced. For the moderately active person 2000 calories is as a rule proper. When he does not lose weight on this allowance it often means that he is eating more than he admits. The greatest restriction should be of fatty and starchy foods. There is no valid reason why the protein of the diet should be unduly restricted. It should approximate 1 gm. per kilogram of ideal body weight or perhaps just a little less, say 60 to 70 gm. daily. Fruits and green vegetables should form an important part of the menu. Because of its salutary value a small amount of something sweet may be permitted at the end of the chief meal. It is customary, although the constituents of this may be open question, to advise that no salt be added to the food after it comes to the table and that no unusually salty food be eaten. This permits about 2 to 3 gm. of sodium daily. When the desired weight loss has been accomplished the food allowances should then be readjusted to form a permanent one.

When a better understanding of the causes of essential hypertension has been obtained a surer dietary approach to the disease will

probably be seen, but there is no clear approach today Until this understanding comes it can properly be assumed that the best diet for the hypertension patient is one that throws the smallest burden on his metabolism and preserves longest his strength and vigor

CIRRHOSIS OF THE LIVER

The outlook is much better in the treatment of another long-term illness, cirrhosis of the liver The liver has great powers of regeneration and, following the discovery that adequate nutrition notably in respect to protein facilitates repair, dietary measures that promote reversal of the pathologic process were devised The results have been little short of dramatic Less than a decade ago it was thought that protein was harmful to the sick liver, and to promote repair carbohydrate was given in large amounts Now protein is given in hitherto unheard of quantities Mann[6] first showed that the liver is best prepared to meet stress and strain when its stores of protein as well as of carbohydrate are ample, and this has been confirmed by others Clinical application of this discovery was first made by Patek and Post[7] who, with a diet of about 3000 calories in which was included 116 to 135 gm of protein, accomplished results definitely beyond expectation in the treatment of cirrhosis of the liver The diet used by Morrison provided even more protein, 200 to 300 gm daily, and surprisingly good results were seen Cirrhosis patients treated at the Hospital of Rockefeller Institute[8] showed like improvement on a diet high in protein and rich in carbohydrate, but credit for the excellent results was given chiefly to the appetite-restoring effects of crude liver extract

The diet used today provides about 3000 calories and includes 200 to 300 gm of protein To restrict the fat, little if any cream and butter are permitted and no other fatty foods, no fat meats, no gravies, no oil dressings To provide requisite calories, relatively large amounts of carbohydrate should be taken, say 750 to 800 gm daily, some of which must be in the form of fruit juices and other sugary foods To provide the required amount of protein the diet should include not only liberal amounts of meat, but large quantities of other foods rich in protein, notably dry skim milk This last is given a prominent place in the diet, 2 quarts or more of reconstituted milk or of fresh skim milk to which milk powder has been added may be given each day

An important feature of this regimen is the administration, not only of polyvitamin mixtures, but also of crude liver extract The latter, to which thiamine is added, should be insisted upon and should be given in fairly large quantities The highly refined extracts are apparently of no value The extract intended for intramuscular use will suffice, but a

preparation of crude liver extract recently designed for intravenous use is more potent The difficulty in the use of this last is that untoward reactions, some of them distressing, are occasionally encountered The administration of liver extract should be continued as long as the patient is under treatment Thus, in a disease that was formerly regarded as invariably fatal unexpectedly happy results are being accomplished with a liberal caloric regimen, high in protein and low in fat, which includes also large quantities of vitamins

PSYCHOSOMATIC DISORDERS

Disorders of psychosomatic origin often demand dietary consideration Even the overeating by a fat person is attributed to emotional vagaries To induce him to eat less it is preferable, I am satisfied, to depend upon persuasion and mandatory authority rather than upon drugs that curtail the appetite If the physician lacks the authority and the patient has not sufficient stamina to effect a reduction in the amount of food eaten, then I think the case is well nigh hopeless

The reverse of this picture is seen in the inanition sometimes portrayed by nervous patients Psychosomatic disorders obviously are accompanied by the widest variety of discomforts, many of which arise in the digestive tract and can be relieved by improvement of the nutritive state Lack of food makes the patient nervous, nervousness impairs his digestion and indigestion causes him to eat less If often helps to explain to the patient that he is in a vicious cycle and that he can break the cycle only by means of a radical change in his food habits he needs more and better food True, concessions must sometimes be made to the patient s idiosyncrasies, notably to the intolerance for roughage seen in the so-called irritable colon and to the discomfort caused by milk in a few people but such concessions should not be carried too far

Neurasthenia is sometimes the initial stage of pellagra and often the disorder does not go beyond this stage This is true also to many other deficiency disorders It has been found that in many types of vague illness remarkable cures can be accomplished if the patient is placed in the hospital and given an abundant diet It is not the rest or the seclusion or the opportunity for quiet contemplation or the pat on the back or the attempted psychotherapy that cures these patients It is the food

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THE PATIENT WITH LONG-TERM ILLNESS AS A SURGICAL RISK

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The mortality associated with surgery in patients who have illnesses of long duration is such that these patients should be evaluated and prepared preoperatively with the utmost care. Since surgical mortality is considerably less in those patients whose physiological status of the body as a whole is normal or nearly normal, every effort should be made to correct any physiological abnormalities before operation and to guard against the development of such abnormalities during and immediately after operation. The evaluation is oftentimes difficult because it may not only be necessary to evaluate the adverse physiological effects of the primary, chronic disease, but it may also be necessary to evaluate possible adverse effects of an acute or secondary disease. This, of course, depends upon whether the surgical procedure contemplated is necessitated by the original, primary illness or by an intercurrent, secondary disease. Many chronic illnesses temporarily or permanently reduce the functioning capacity of vital organs. In this respect the patient with an illness of long duration may resemble the geriatric patient. Attempts to correct existing physiological disorders should be carried out cautiously because of the reduced ability of many of these patients to withstand vigorous therapy.

The evaluation of the patient with a long-term illness for surgery therefore should not only include the status of nutrition, fluid balance and electrolyte balance, but it should also include the functional ability of the cardiovascular system, respiratory system, liver and kidneys to withstand sedation, possible intravenous therapy, anesthesia and operative trauma. In addition, the postoperative complication of thrombo-embolism, which is frequent in the type of patient under discussion, should be actively guarded against.

MALNUTRITION

The importance of malnutrition in relation to surgical morbidity and mortality continue to receive increased emphasis in the surgical literature today. Although much remains to be learned regarding nutrition, considerable knowledge was gained during the recent war. It is probably fair to say that surgeons in general have been slow to recognize the importance of adequate nutrition in the patient who is to undergo surgery, especially in regard to the patient with an illness of long duration.

* [illegible]

Protein depletion alone may adversely affect the surgical patient in many ways In addition to the well known delay in the healing of most types of tissue and the tendency to produce edema, hypoproteinemia predisposes the patient to shock, infection, liver damage, anemia, hypomotility of the gut, hypocalcemia, increased blood urea nitrogen and perhaps the deficient formation of prothrombin

Hypoproteinemia leads to a reduction in blood volume and therefore moderate degrees of psychic trauma, physical trauma or blood loss may precipitate shock in the hypoproteinemic patient Cannon[1] has demonstrated the role of adequate protein nutrition in the prevention of infection He has pointed out that hypoproteinemia is one of the main clinical findings in patients dying from various types of chronic diseases and that secondary infection is common in those patients Experimental animals on a diet adequate in all respects except protein develop spontaneous infections Cannon and his associates[1] have demonstrated that a protein deficiency is associated with a lowered activity of the antibody-producing mechanism and that the restoration of the depleted protein reserves of the body results in the restoration of the normal capacity for antibody production They have also pointed out that in severe inanition the cellular tissues, which in the presence of infection ordinarily supply phagocytes in large numbers, undergo atrophy Such atrophied tissues are not advantageously prepared to cope with acute infection by the liberation of adult phagocytes regardless of the amount of specific antibody which may be present [2] Cottingham and Mills[3] report that dietary deficiencies of protein and certain vitamins namely, thiamine, pyridoxine, riboflavine, ascorbic acid, choline and pantothenic acid, in young white male mice may all depress phagocytic activity of the polymorphonuclear leukocytes in vitro Thus, malnutrition may embarrass two of the body's biologic mechanisms against infection Under such circumstances an infection which might ordinarily be of minor significance may become of serious importance

It is impossible in this presentation to list and discuss all of the adverse effects of even the single nutritional deficiency of protein in the surgical patient, much less to discuss the known adverse effects of deficiencies of other nutritional elements The adverse effects of nutritional deficiencies are greatly multiplied in clinical practice for rarely, if ever, does a patient present himself with a deficiency of a single nutritional element

The common causes of malnutrition in surgical patients include (1) inability to ingest or retain food in the presence of nausea or vomiting, (2) inability to digest and assimilate food due to disease of part or all of the gastrointestinal tract, (3) chronic infection, (4) severe trauma, (5) wasting noninfectious diseases including carcinoma, (6) ill advised

special diet assumed by the patient or prescribed by a doctor, (7) inability to obtain food, and (8) of course, lack of appetite for any reason In response to the physical and "physiological" trauma of operation and anesthesia, it should be realized that the body as a whole shows evidences of loss of important nutritional elements It has been demonstrated that there is a decrease in the ascorbic acid concentration in the plasma in direct proportion to the magnitude of the operative procedure performed [4] Levenson and his associates,[5] in a study of acutely ill patients found abnormally small amounts of ascorbic acid in the plasma and abnormally small amounts of ascorbic acid, thiamin, riboflavin and nicotinic acid in the urine They interpreted their studies as lending further support to the idea that large doses of ascorbic acid, thiamin, riboflavin and nicotinic acid may serve a useful purpose in the care of acutely ill people Major surgical operations are associated with a decrease in serum protein concentration postoperatively [6, 7] There is a marked loss of protein substance of the body following fractures of the long bones [8] The weight loss associated with major operative procedures, severe trauma and burns is not infrequently 1 to 1½ pounds per day [9, 10, 11] Ether anesthesia, the barbiturates and morphine cause a decrease in the prothrombin time [12] It is not definitely known whether the relative deficiencies of protein and the vitamins after operation and anesthesia represent increased utilization of these substances, increased breakdown of these substances for the formation of other essential substances or body wastage during periods of stress

Preparation of the Surgical Patient in Respect to Malnutrition — Since adequate nutrition is most efficiently attained by the oral route, every effort should be made to provide and encourage the patient to eat a more than adequate amount of food when possible To simple request an adequate food intake is not enough Special nursing care may be necessary The cooperation of a dietitian in the hospital is often of the greatest help in making the food more palatable to the patient and also in making food available at other than the regular mealtimes

Parenteral or intravenous nutrition may be used to supplement oral feedings or it may be the only form of nutrition possible for certain patients However it should always be remembered that protein taken by mouth is more efficiently utilized than its equivalent administered as a protein hydrolysate solution intravenously It should be realized that the protein preparations generally available for intravenous use at the present time are protein hydrolysates and as such represent a mixture of peptides and amino acids and are not pure amino acid solutions The available data regarding the utilization of parenteral protein hydrolysate preparations are based chiefly upon the retention of these substances in the body i e a positive nitrogen balance There is a lack of scientific

evidence as to just how much of the injected and retained protein hydrolysate is actually utilized by the body in the form of protein or amino acids [13]

When the oral route cannot be used, one must, however, resort to parenteral feedings regardless of how efficient this method may be It should be remembered that 3000 cc of a 5 per cent solution of glucose administered intravenously in twenty-four hours will actually provide approximately 600 calories per day If glucosuria is produced, the caloric intake would be less than 600 calories Such a caloric intake represents barely one-third of the daily caloric requirement of an healthy adult at rest in bed The average surgical patient with accidental trauma, surgical trauma or infection requires more than basic caloric needs Protein digests or protein hydrolysate solutions administered intravenously under such conditions will probably not contribute to the correction of hypoproteinemia but may help to prevent further intensification of the hypoproteinemic state and probably help to overcome the daily caloric deficiency When the daily caloric requirements of the patient cannot be satisfied by intravenous glucose and protein hydrolysates, a protein deficiency certainly cannot be overcome by such injections With the use of glucose and protein preparations intravenously, no one has been able to maintain a surgically ill patient in nitrogen balance over a period of even several days Thus if the predisposing factor to malnutrition still exists, it is foolish to expect that parenteral protein hydrolysate feedings will improve nutrition before operation Elman[14] has calculated that an oral intake of 375 gms of protein per day for 10 days is necessary to overcome a chronic hypoproteinemia in which the serum protein level is depressed 2 gm per 100 cc below the normal level Rarely is it possible to have a patient take consistently more than 150 to 200 gm of protein by mouth day after day Recent studies indicate that the total amount of protein required may be even greater than Elman has anticipated, for the serum protein level is not an accurate measure of the protein depletion of the body as a whole, according to Lyons and Mayerson [15] Many chronically ill surgical patients cannot or will not injest large amounts of protein over periods of several weeks, and, of course, in many patients operation cannot be delayed for this length of time Also the economic factor of long periods of hospitalization cannot be overlooked

How then can one rapidly prepare the surgically ill patient with malnutrition and hypoproteinemia for operation? Oral intake, if at all possible, should be utilized to the fullest extent Gastric intubation for the administration of nutrient, liquid-food mixtures may be alternated with oral feedings or may be used as the sole method of nutrition Intravenous feedings may also be used to supplement the oral intake or they may be the only form of nutrition when the oral route cannot be

used The greatest benefit in the shortest period of time, however, would appear to result from the use of whole blood transfusion Lyons and Mayerson have shown that surgical patients who have lost 10 per cent or more of their body weight are greatly benefited by the administration of large amounts of whole blood They have found this to be true in spite of the fact that the determined hemoglobin levels and the serum protein levels may be normal or nearly normal for these substances Apparently one of the first responses to a reduced number of circulating red blood cells and a reduction in the total amount of serum protein is a reduction in total blood volume Thus relatively normal hemoglobin levels, red blood cell counts, and serum protein values may be obtained in the patient with a reduced total blood volume, a reduced total serum protein, and a reduced circulating red blood cell mass Lyons and Mayerson have found that the average adult surgical patient with a weight loss of 10 per cent or more of body weight can receive on the average of 2700 cc of blood preoperatively at the rate of 1000 cc per day Patients so treated, in his experience, have had a shorter period of convalescence, a greater sense of well being and better wound healing than similar patients who did not receive such vigorous therapy It would thus appear that for the adequate preparation of the chronically ill patient with hypoproteinemia for operation, the oral route should be used if this route is available and if the operation can be delayed for several weeks or more, but the greatest benefit in the shortest period of time will result from liberal blood transfusion

Supplementary vitamins should be administered to the patient with poor general nutrition A daily minimum of 100 mg of vitamin C, 50 mg of nicotinic acid 10 mg of thiamine hydrochloride and 5 mg of riboflavin should be administered orally or parenterally to these patients If an actual deficiency is present or even suspected, therapeutic doses should be administered for at least several days and then followed by the minimal dosages described Lawenson and his co workers[3] have shown that patients following major operations, accidental trauma or burns may utilize as much as 1 gm of ascorbic acid and 500 mg of thiamine daily to insure adequate plasma levels of these vitamins If the vitamins cannot be ingested or assimilated by the gastrointestinal tract they can be divided and administered in the intravenous solutions or blood administered in a given twenty four hour period Admittedly a great proportion of the vitamin preparations used today are wasted, but where the need exists or where there is a suspicion of subclinical vitamin deficiencies more than adequate vitamin therapy should be used When methods are available to assay one for the determination of the amount of the various vitamins present in the body and we are better equipped to interpret the values so determined the vitamin preparations

tions can probably be used more efficiently In the meantime, we must assure ourselves that our patients are not deficient in regard to vitamins, for there are many adverse effects not only of clinical but of subclinical deficiencies of the vitamins in the surgical patient

DEHYDRATION

Patients who have been ill for a considerable period of time may exhibit the effects of dehydration Dehydration may (1) produce inadequate elimination of products of metabolism of the body, (2) produce acidosis (especially in infants and children), (3) aggravate the seriousness of a reduced blood volume secondary to malnutrition and hypoproteinemia, (4) interfere with the temperature regulation of the body, and (5) delay wound healing The clinical indications of dehydration are (1) excessive thirst, (2) dry tongue and mouth, (3) loss of tissue turgor, (4) dry skin, and (5) concentrated urine of small volume Coller and his associates[16] have stated that, when the clinical signs and symptoms of dehydration listed are present, the patient can safely be given the equivalent of 6 per cent of his body weight in fluid It should be remembered, however, that dehydration of the tissues is one of the processes of aging, and therefore the normal skin of the elderly patient will be drier and will have decidedly less turgor than the skin of younger individuals

If an attempt is made to hydrate rapidly a previously healthy patient with severe dehydration, the adult weighing 40 kg can be given 2400 cc of fluid in addition to his daily requirement of 3000 cc of fluid Such a patient, exhibiting the clinical signs and symptoms of dehydration described, could thus receive 5400 cc of fluid over a period of twenty-four hours without danger of overloading a normal cardiovascular system Obviously, there are some exceptions to this rule as in the case of patients with severe hypoproteinemia secondary to malnutrition When malnutrition, hypoproteinemia and dehydration are present, the hypoproteinemia and malnutrition should be treated simultaneously, for the administration of large amounts of fluid may precipitate clinical edema and may cause further embarrassment of function of vital organs In the chronically ill patient and when in doubt, the dehydration should be overcome gradually, and the calculated amount of fluid should be divided and administered over several days as fluid added to the patient's daily requirement of fluid

The fluid used to overcome dehydration should be in the form of 5 per cent glucose in water Physiological saline solution should not be used indiscriminately unless there is a definite indication for salt as determined by chemical analysis of the serum, whole blood or urine Following the use of sodium chloride solutions, the kidney does not freely excrete

all of the excess sodium, chloride and water Edema may thus be produced [15] It has been shown that even a small excess of sodium chloride at times may be injurious to the kidney Physiological saline solution is therefore administered only when definitely indicated It is probably better to err slightly in giving too little intravenous sodium chloride rather than to give too much

THROMBO-EMBOLISM

Thrombo-embolic disease is more prevalent in the elderly patient and in the patient with a long-term illness All possible means, therefore must be taken to prevent the development of venous thrombosis When thrombosis does develop, steps should be taken immediately to prevent the formation of emboli Prophylactically, it is important to discourage positions in bed and any type of bandage which tends to produce venous stasis, to encourage early motion and early ambulation, and to prevent dehydration The use of adequately applied elastic bandages to the legs may compress superficial veins but do prevent stasis and help to prevent the formation of thrombi in the larger deep vessels In addition, slowing of the flow of venous blood by any mechanism and the increased viscosity of the blood resulting from dehydration favor the formation of thrombi

In spite of the recent widespread interest in the serious problem of thrombo embolism, it would appear that at the present time we do not know the final answer to the therapy of thrombo embolic disease The two main schools of thought are along the lines of (1) the use of anticoagulants and (2) femoral vein or other venous ligations Some of the difficulties of anticoagulant therapy lies in the close supervision required and the necessary close cooperation between the clinician and the laboratory Hemorrhagic complications, pulmonary emboli and an occasional death do occur with the use of anticoagulants, especially in elderly patients Ligation on the other hand does not prevent the formation of thrombi and emboli above the level of ligation and occasionally there is chronic embarrassment of the circulation distal to the level of ligation even following ligation of the superficial femoral vessel

For some time the general rules outlined in Table I have been followed at the Hospital of the University of Pennsylvania In the way of prophylaxis the following factors are important (1) prevention of dehydration (2) correction of electrolyte imbalance (3) replacement of blood loss (4) regular leg and breathing exercises (5) elastic bandages to the legs (6) avoidance of abdominal distention (7) avoidance of pressure under popliteal space, (8) bed exercises, and (9) early ambulation Prophylactic anticoagulant therapy and prophylactic ligations are used only in

patients in which the risk of thrombo-embolic disease seems unusually great and then are used only on the approval of the respective chiefs of the surgical services

Acute thrombophlebitis with classical symptoms of increased pulse rate, increased temperature, local tenderness, swelling and discoloration of the skin of the affected extremity is treated with repeated lumbar sympathetic blocks Mild thrombophlebitis or phlebothrombosis with pulmonary infarction as demonstrated by clinical symptoms of pleural pain, blood tinged sputum or x-ray evidence of pulmonary infarction are treated by bilateral superficial femoral ligation If there are repeated infarcts after ligation or evidences of extension of thrombi proximal to

TABLE 1

THERAPY OF THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS

I Conservative prophylatic therapy—all patients
II Ligation
  1 Phlebothrombosis—bilateral superficial femoral ligation
  2 Suppurative disease of iliac or pelvic veins or vena cava—ligation above area of suppuration
  3 Pulmonary infarction—bilateral superficial femoral ligation
III Anticoagulants
  1 Thrombosis proximal to superficial femoral vein
  2 Repeated pulmonary infarcts after ligation of superficial femoral veins
IV Lumbar sympathetic block
  1 Acute hrombophlebitis

the superficial vein, anticoagulants are used Ligation of the iliac veins or the inferior vena cava is reserved for suppurative ileofemoral or pelvic thrombophlebitis (Table 1)

DIABETIC PATIENT

The possibilities of acidosis, insulin shock, coma, poor wound healing and infection require that the diabetic patient be carefully managed before and during any surgical procedure Surgical emergencies may require vigorous treatment of the diabetes, perhaps without complete preoperative control of the diabetes, in order to make the patient satisfactory for surgery Whenever possible the services of a consultant experienced in the management of diabetic patients should be enlisted It should be remembered that diabetic acidosis alone may produce the signs and symptoms of an acute abdomen and lead to an unnecessary operation These symptoms may persist for as long as seventy-two hours after the diabetic acidosis has been overcome If the implications of the patient's history and physical findings are such that delay of operation may prove to be injurious, exploratory laparotomy may be performed

when the urine is acetone free Uncontrolled diabetic or poorly controlled diabetic patients are very susceptible to infection The infection itself has a deleterious effect upon the diabetic status, and therefore patients with infectious processes may require more insulin for the control of diabetes in the presence of infection than the same patient would require in the absence of infection It has been shown experimentally that the rate of wound healing is not impaired in the diabetic patient provided acidosis is not present It would appear then that wound healing is not seriously jeopardized at least until acidosis is present

When diabetic acidosis is present, strenuous efforts should be made to overcome the acidosis almost regardless of the serious implications of the abdominal signs The urine should be acetone free before operation is undertaken Patients with acidosis requiring urgent operation should be treated vigorously with insulin and oral and intravenous carbohydrate The methods of treatment used in the control of diabetic acidosis will vary somewhat with the experience of the person treating the patient However, the administration of fluid, carbohydrate and insulin form the basis of all types of therapy Intravenous glucose by continuous drip should be administered to those patients who cannot take adequate amounts of carbohydrate by mouth or those patients who will have a general anesthesia and who should not take anything by mouth Urine specimens are examined punctually every two to three hours as the urgency of the situation demands If there is the least suspicion of urinary retention from one period to the next, catheterization should be used to insure that no acetone is retained in the bladder from one period to the next A temporary indwelling catheter will eliminate repeated catheterizations Blood sugar and plasma carbon dioxide determinations should be done immediately Although the blood sugar level and the serum carbon dioxide value will indicate the severity of the acidosis and the probable duration and intensity of treatment required before acetone-free urine is obtained, in the absence of comm the results of the urinalyses may be used as the guide to the insulin dosage In general with a 4 plus glucosuria and a 4 plus acetone determination, 25 units of regular insulin is administered For 3 plus acetone 20 units 2 plus acetone, 15 units, and 1 plus acetone 10 units of regular insulin are administered Sufficient glucose should be administered to cover all insulin administered to the extent of 2 5 gm of glucose for each unit of insulin Too little glucose may lead to insulin shock whereas a moderate excess of glucose leading to 3 or 4 plus glucosuria is not harmful When diabetic coma is present of course the indicated dose of insulin is much larger sometimes as high as 100 or 200 units in the first three hours The important immediate considerations are to obtain and maintain the patient with acetone free urine and guard against insulin shock

For elective operations on controlled diabetic patients, regular insulin and fruit juices fortified with glucose may be administered until four hours before operation For patients who cannot take liquids in the immediate postoperative period intravenous glucose and insulin, in a ratio of at least 2 5 gm of glucose to each unit of insulin, can be administered by continuous intravenous drip In the presence of accidental trauma, surgical trauma or infection, the twenty-four hour total requirement of insulin may be increased over the previously established twenty-four hour insulin requirement Thus a patient who cannot take fluids by mouth postoperatively and who has been previously standardized with 40 units of protamine insulin (or total protamine and regular insulin units) can be maintained with 3000 cc of 5 per cent glucose to which has been added 50 units of regular insulin Thus in twenty-four hours the patient would receive 150 gm of glucose and 50 units of crystalline insulin—a ratio of 3 gm of carbohydrate to each unit of insulin—by constant intravenous drip Fractionated urinalyses and blood sugar determinations should, of course, be done before and after operation and continued until the diet and insulin dosage is again standardized If the patient is receiving intravenous glucose, the blood sugar determinations will be useless, however, if the urinalysis shows glucose and no acetone, one can be certain that sufficient insulin and more than adequate glucose are being administered There is no evidence that marked glycosuria is harmful to the diabetic patient during the operative and immediate postoperative period In fact, many diabetic authorities during the past fifteen years have become more and more liberal in regard to the amounts of carbohydrate allowed their patients

The use of chemotherapeutic and antibiotic agents in diabetic patients has reduced the mortality and morbidity of operative procedures Although it should not be the general rule, it is often possible to delay operation in the presence of infection of the extremities, and it is often possible to do less extensive operations with comparative safety if the circulation appears to be adequate With the use of these antibacterial agents more latitude is therefore possible to the surgeon in the treatment of the patient Thus before sulfonamides the practice was to treat infected arteriosclerotic extremities as emergency surgical cases The surgical procedure was carried out immediately, and amputation was carried out in an area where the circulation was certain to be adequate, usually a mid- or a low-thigh amputation With the use of chemotherapeutic and antibiotic agents it is frequently possible to do a local amputation without undue risk and with the realization that a more radical amputation may become necessary at a later time

GERIATRICS

With the steadily increasing number of people in the United States over the age of 65 years, an increasing number of patients of the older age group confront surgeons

Recent experience has taught that many elderly patients withstand operation very well Why do some respond better than others? It is well recognized that chronologic old age is not synonymous with biologic age Some people are old at the age of 40 and others are young at the age of 70 The active patient with thin, dry and tough skin, clear voice, bright eyes, strong will, good appetite and an interest in his surroundings, is young in regard to his physical state regardless of his years of life On the other hand, the feeble patient with soft skin, weak pulse, weak stomach and little interest in his surroundings may be physically older than his stated years would indicate

It has frequently been said that the principles of surgery and anesthesia must be altered in respect to the age of the patient Strictly speaking, this is not true Surgical principles, if they are sound principles, are sound regardless of the age of the patient The application of these principles, however, may require modification for the elderly patient Modification is necessary because the geriatric patient is not as adaptable as the young patient and therefore many types of therapy cannot be as vigorous in him As one of the normal processes of aging, the so called reserve functioning capacity of vital organs such as the lungs, the heart, liver and kidneys is reduced by the repeated insults of ordinary life over a period of many years In this sense, an illness of long duration or repeated illnesses may bring about premature aging in a chronologically young patient The peripheral vascular system is less elastic and may be sclerotic, and therefore the cardiovascular system is poorly able to combat situations which tend to produce hypertension or hypotension The elderly patient with an abnormally reduced blood volume or with abnormal dehydration may not be able to withstand the injection of blood or fluid at the rate it would be administered to a younger patient, regardless of the need for blood or fluid Usually in the absence of an emergency, the blood and fluid needed can be administered cautiously over a period of several days Ordinary medications and anesthetic agents which tend to cause a fall in blood pressure should be avoided if possible In addition, the decreased metabolic rate, another result of the processes of aging, profoundly alters the elderly patient's response to therapy especially in regard to some types of medication The reduced reserve of the liver and kidneys usually associated with advanced age are also probably responsible for the profound depression and prolonged action of certain narcotics and barbiturates

Anesthesia—Adequate preoperative preparation of the young individual will allow the use of a wide choice of anesthetic agents The choice of anesthetic agents for the elderly patient is more restricted, and the agents used must be administered with discretion Although an individual anesthetist may have special likes and dislikes in regard to anesthetic agents for elderly people, the following statements are agreed upon by many anesthetists

Ether anesthesia is not a desirable anesthetic in elderly patients because of (1) long induction, (2) long recovery, (3) excessive secretion, (4) coughing, and (5) retching Cyclopropane is the best volatile anesthetic agent for these patients since it is less toxic to tissues and since it possesses 100 per cent potency Nitrous oxide is the poorest of all anesthetics in elderly patients because its potency is only 15 per cent of stage III anesthesia Oxygen should be used with all forms of anesthesia in elderly patients Ethylene is good for operations of short duration and minor nature Chloroform should not be used because of its toxic effect on the heart, liver and kidneys The dose of preanesthetic medication should be less than that usually used for younger adults Thus, patients over 60 years of age, as a rule, should receive minimal amounts of sedation to avoid the profound depression often observed in these patients with the usual dosage of medication Spinal anesthesia can safely be used in many nonhypertensive elderly patients if adequate measures are used to prevent and combat the effect of hypotension

Whenever possible, enemas are to be avoided in the elderly patient because of the possibility of precipitating a catastrophe such as a cerebrovascular accident or a pulmonary embolus The routine order of administering an enema preoperatively to geriatric patients therefore should be questioned Frequently, when the patient has eaten little or nothing several days before operation and the rectum is empty by digital examination, the enema can safely be omitted In other instances cathartics (not drastic) should be used in preference to enemas whenever possible

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PLANNING FOR LONG-TERM ILLNESS

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INTRODUCTION

PLANNING for prolonged illness beyond the acute phase is an obligation imposed on us by varying pressures from several directions in recent years. These are, broadly: (*a*) the requirements of the social security program, which has exercised a beneficent influence on the civilized life of our generation, benefiting the underprivileged—including the medically underprivileged—and guaranteeing an irreducible minimum of subsistence during unemployment, illness, old age, or other kind of dependence; (*b*) the increased tempo of scientific—including medical—invention and discovery, under which additional worlds are being sought for conquest by men whose skill, imagination, and, in particular, patience, are being rewarded in the field of long term (chronic) illness; (*c*) the increased span of life, with the Biblical three score and ten already achieved, creating and multiplying new and compelling problems which must be faced by society when age, allying itself with pathogenicity, prolongs and often complicates it in a slow, insidious, and relatively unresponsive course of illness or discomfort; and (*d*) the conscience of humanity, which can no longer tolerate the anachronistic distinctions which are translated into medical selectivity when men are sick, unhappy, uncomfortable or dependent, and is demanding a more searching study of cause and effect for everyone, under all circumstances, by men working with adequate tools and competent to draw useful conclusions.

On the other hand, these pressures are subject to varying resistances from opposing directions. These restraining influences are related to (*a*) the inflationary money values of our day which have been increasing the spread between hospital income and expenditure and leaving operating deficits traceable in large part to them; (*b*) the relatively high cost of medical progress which results from intensive care with the use of expensive diagnostic and therapeutic procedures; (*c*) a shortage of trained personnel for specialized tasks; (*d*) the unavailability of the additional space which is needed to serve each hospital bed; (*e*) vested interests, some rigid as in the case of existing hospital buildings, others paradoxically flexible yet equally unyielding, and (*f*) communal and political inertia often due to unawareness of the trends in health and medical care. These thoughts are expressed in the principles and practice of social medicine, the latest and best of the combined specialties which

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takes for its province the whole man, in relation to his environment and to the spirit which animates him

Many of the current trends of public health and medical practice are the direct or indirect results of the interaction of these broad phenomena Health and medical care, known in the curriculum as preventive and curative medicine, started as a unit, separated in an effort to develop undisturbed, then overlapped, and are now yielding to the necessity of working side by side toward a common goal It is characteristic of our time that diagnosis and therapy in the preclinical and clinical states are considered to be inseparable in the sickroom, in the experimental laboratory and in the lecture halls of hospitals and medical schools The so-called "diagnostic" specialties are not boastful of the designation, under which they have been living an incomplete existence This being the case in advancing measure, it is natural for the general and the special in medical care to reunite We are moving into an era when more and more of the achievements of medical practice and medical organization will be available for the management of prolonged illness Group medicine can now be practiced with the object of exhausting every diagnostic precision instrument and therapeutic modality in a search for etiological factors and complete restoration to individual health It is on the principle of group medical practice that the modern general hospital has been founded Since we are living in an age that is strongly affected by long-term illness, no physician, acting alone, can hope to do more than advise and coordinate in the more difficult clinical situations which confront him, while dealing directly with the simple problems which yield readily to his efforts

Continuity of service is another trend which is unmistakable Because of it, in-patient and out-patient will be treated continuously, as a unit, and the clinical biography of the patient will then be a logical sequence of facts, figures and graphs presented to the student in an unbroken picture As we shall see in the following pages, short-term (acute) illness and long-term (chronic) illness are similarly approaching continuity of the medical service which they require There will be less tendency to make distinctions between them where none should exist Moreover, they will be dealt with in one location instead of two that are widely separated

When one adds an extramural hospital program for the care of selected patients at home, to carry out the principle of continuity of effort, the overall picture becomes clearer and the hospital comes at last into its own as the central facility of its community in health and in disease

All of this is based on the assumption, which is finding greater justification as the years pass, that the practitioner of medicine is a man of science and that he produces his best work when he is dealt with and

encouraged that way. His never-ending source of continuing medical knowledge is the modern hospital, which does, indeed, stand between him and the cults. Because the physician is a man of science, we are establishing or increasing space allocations in hospitals for lecture halls, conference rooms, and laboratories for scientific investigation, while seeking talented men, in addition to those we have, who are eager to use them. It is the hospital on which our attention must be focussed. Let us now look at the argument in greater detail.

CURRENT TRENDS AND INFLUENCES IN MEDICAL CARE

Institutional management of the sick in its various manifestations, including the well-defined entity of the hospital, has been elaborated in response to immediate communal need. This need, in its most characteristic form, is expressed in terms of medical and social urgency. Organizational revisions, and adjustments to change are, however, characteristic of social progress and continue at work. We are now faced with the *urgent* problem of long term (chronic) illness and organizational changes are under consideration everywhere. This is due to the fact that *acuteness may wear off long before the sickness is brought under control.*

Highly organized hospitals, ultimately based on the principle of group practice to give the patient the benefit of any doubt, and to keep individual members of the group informed, were established for the care of the *urgent case*. Their sponsors have thus far complained when the nonurgent, after acuteness wore off, continued to occupy beds which might have been assigned to them as a result of bad judgment on the part of the admitting officer as to prognosis in connection with duration of illness. Additional institutional types, most of them not so highly organized, some retaining the term "hospital" as part of a euphemistic but misleading designation, were then established for those who were not immediately urgent but who were nevertheless a burden on the community. These institutions still follow a catch all policy of communal service as they pick up the leavings after the strictly limited policies of the acute general hospitals have been enforced. Inside of their walls are admitted the overflow, the undesired, and the indigent, and these are still being retained unquestioningly over long periods of time without anyone stopping to reappraise their clinical condition, except in the most perfunctory way. These institutions, giving a custodial type of care, are almost always maintained at the expense of the taxpayer as a kind of compulsory philanthropy. The quality and quantity of this care, in most cases, bear an inverse ratio to the length of stay of the inmates: the longer he stays the less his medical care, whereas this should bear a direct ratio to the need for such care.

We are now being confronted with the necessity for a realignment of social and medical forces to meet enemies to health and comfort with which we can now cope more successfully than ever before, so successfully, in fact, that *our conquests are producing rapidly a shift in emphasis from the "acute" to the "chronic" patient* As a motivating-force in the planning of medical care, the response to urgency (in the sense that the patient compels immediate attention) varies in extent, variety and promptness In a qualitative sense, the need today may not be strikingly different from that of a former generation but many more methods are now available to us to meet this need *Medical science and medical organization have more and more to offer the sick* Hospitals in the prescientific era flourished largely because they provided a form of housing during illness that was superior to the poor man's home They had little else to offer It is much more than a matter of housing today, though *housing often compels our decisions, as a form of social pressure, even when an intensive form of scientific care in a hospital is not indicated*

The convenience of the physician is another factor which influences the organization of medical care since the concentration of his patients in one location simplifies his problem of rounds and enables him to dispose of more in a shorter period of time There are, however, better ways now available to achieve the same result in cases which obviously do not require transfer to a hospital

The spirit of mutual aid which determines the man of means to share his bounty with his luckless neighbors exercises a powerful influence on his reaction-time in responding to urgency Many members of the wealthier classes enjoy public approval because of their generosity in establishing institutions for the sick and the helpless Here we find the ingredients for a social formula which has always protected the interests of the sick—medical and social urgency, philanthropic (including religious) response, and the progressive impact of an advancing medical science on both The compounding, dosage and timing of this prescription, so that every patient will have administered to him the right dose of the right medicine at the right time, interest the planner at every step

For a long period, as long in fact as it took the science of medicine to develop, the best response was represented in a practical way by the acute general hospital, which took over from the patient's home as a court of last resort Since this kind of hospital mobilized, unified and made available the best of all diagnostic and therapeutic arrangements required to relieve signs and symptoms, it was considered quite justly the pacemaker for all medical effort and the aristocrat of institutions, and got the lion's share of credit for medical progress Here, par excellence, was a clinical laboratory which had the added advantage of permitting a certain amount of experimentation under the highest possible

auspices It was in this kind of institution that the student was to be found, for nowhere else could he learn as quickly, in as highly concentrated a program, or as successfully Cases in series, more readily available where larger numbers of patients were assembled under a superior grade of medical practice, yielded sounder conclusions than could be drawn by the practitioner working independently of the hospital

However, the scientific world marches on Hospitals move to higher levels of service, and so do community plans for housing which take into consideration the need for progressive improvement in sanitation and in facilities for reasonable isolation during illness The span of life is increasing and it is being accompanied by startling social implications We have discovered of late that *we will have to live longer with each other in health and in illness That this will affect the problem of hospitalization is something that the town planner should ponder quite as much as the hospital planner* Institutional facilities, vis a vis the home, can now be rearranged and redistributed and new construction planned in accordance with the new trends As new medical (and social) horizons come into view and as scientific interest is attracted to the origin of signs and symptoms as well as their relief, we find a diminishing tendency on the part of acute general hospitals to fret over patients who do not have, or lose, the power to contribute their share of financial, *or clinical*, currency which sustains the hospital and its medical staff respectively The average stay in such hospitals has, indeed, been shortened progressively so that it is now only eight days Beds are therefore being used more intensively for the greater good of the greater number The competition between the bed in the hospital and the bed in the patient's home, which has had so much to do with the development of hospital programs through the ages, is shifting and *the burden of care, during illness which does not require the high concentration of hospital facilities, is returning in large part to its point of origin—the home*

The best hospitals with a few notable exceptions have been those which were labeled as acute general hospitals and of these most have been in the voluntary (philanthropic) classification They have been by far and away, the most productive scientifically, even though they have felt compelled to keep the challenging long term patient at arm's length and shifted the burden of his care elsewhere at a time when he may have needed it most The qualifying term 'acute' points up the response to urgency and medical desirability which motivate these hospitals *Urgency, however relates to signs and symptoms and not always to underlying pathological social and medical conditions* Let there be any doubt as to the subject of acuteness and the applicant for these prime services is too often denied admission with no other adequate medical resource at his disposal

Age, too, influences his chances, for the older the patient and the longer his medical history the greater the probability that acuteness, which does not always respond rapidly to treatment, will wear off and be replaced by stubborn chronicity The chances for complications, sequelae and relapses are also greater in proportion to the life span and the admitting officer is aware of this during the course of a day in which he is too often called upon to make a snap prognosis Duration of illness, which has always been a controlling factor in the appraisal of the applicant for admission to the general hospital, has had a subtle but potent influence on hospital policy, yet *prolonged illness has an inherent challenge which no man of science can safely decline to accept at this stage of medical progress, much less cast off for less talented hands to deal with at a distance from the center of hospital service*

As the classroom and the laboratory make their appearance and improve their status in the modern hospital, and as new plans for its financing are applied, the hospital may be left with a major problem in its efforts to provide full coverage for the sick, and that is the problem of beds Where scientific talent is encouraged, and where money is available for the care of the indigent, enabling the hospital to retain them longer so that interest in prolonged illness may be sustained, there may still remain the problem of a shortage of beds One would think so, at least, from the considerable number of additional hospital beds that were planned in such an expansive mood as a postwar contribution to the health of the public It is the "shortage of beds", often reiterated in the public pronouncements of hospitals, even after the first two motivating factors have been neutralized, that has thus far led to the establishment of other institutions for the sick to take care of all those who are so unfortunate as to suffer from a nonacute condition

Homes for incurables, in many cases deliberately sheltered from public view, were established beyond the horizon where a patient might live out his days as best he could unaided by the march of medical progress The most valuable of all clinical material thus went to waste and the scientist labored or waited elsewhere for therapeutic plums to fall into his lap These institutions still dominate the general picture of medical care for the long-term sick and block one of the important avenues of medical progress by their inactivity and their wastefulness of clinical opportunity

Homes for the aged, similarly, in a philanthropic attempt to improve the housing facilities of the elderly, segregated them from younger relatives who could not tolerate or support them, or agree with their views of life Some of them went further and, like the homes for the incurable, though to a lesser extent, served as dumping grounds for the acute general hospitals which, by this additional outlet for their undesirables,

were encouraged to limit themselves to the care of the acute In recent years the line of demarcation between home for the aged and home for the incurable has almost disappeared They have been showing a common denominator of custodial care

There are also county homes and "hospitals" where the taxpayer often saves the homeless long term sick-poor from death in the gutter, only to prolong an illness which might yield a cure sooner or later if studied under proper auspices Almshouses and poor farms are almost entirely in the same category Another type of institution, which is so often misleading in its public appeal, is the independent hospital for chronic diseases This type of institution is, in reality, patterned on the lines of the home for incurables In these institutions, and their like, the doctor-trustee position is too often a study in social stagnation Somewhat like the relationship between poverty and long term illness, these two are in a vicious circle, each awaiting the day when the other will release its stranglehold or break through with a stimulating program Both groups need the feel of the classroom and the laboratory under an enlightened medical outlook One needs to mention the fact that *there is only one voluntary hospital for chronic illness on a par with the acute general hospital to prove the point* Montefiore Hospital in New York City, which renders a high grade of scientific medical service to its long term patients, has never been duplicated Furthermore, we now know that it never will be, since the line of separation between "acute" and "chronic" is fading away and only appears nowadays as a survival of the prescientific era *Duration of illness per se is no criterion for the admission of a patient to a hospital It is his need for intensive hospitalization that counts and not the question of acuteness or chronicity* This is true even though prolonged illness does not bear the close relation to immediate urgency that acute illness does The claim of the urgent to priority in the hospital cannot be denied but this claim is directly related to the number of beds available Where there are enough beds for all who need them the question need not arise

When an independent hospital for chronic diseases has been organized on a high level of scientific excellence, with classrooms and laboratories to stimulate the development of talented men of science its sponsors soon discover that acute medical episodes are easily and effectively dealt with as emergencies in the same institution It is equally true that the acute general hospital, which commands the best in scientific facilities can readily continue the care of those who still need it, instead of pursuing a policy of transfer, isolation and segregation of such patients

Returning here to the explanation by the acute general hospital that its policy of transfer of the long term patient is due to a shortage of beds we have the always reminder that two beds in one location to take

care of the overflow of scientifically needy patients, is better than one bed in one favorable location and another bed at a distant and unfavorable location As for the danger that medical interest may gravitate from the chronic to the acute in a combined hospital one need only ask himself where the danger would be less to the patient and to the science of medicine—in a planned arrangement where the two share the same facilities or in the older arrangement which separates them? We are dealing in a combined institution with the lesser of two evils but the lesser evil will be progressively reduced as the science of medicine and the art of philanthropy advance under more favorable planning In separate institutions we continue deliberately to place obstacles to the attainment of this ideal for the patient We shall doubtless see a leveling-off process by which acute and chronic (short-term and long-term) in hospitals will unite in one facility as long as the need for a hospital bed can be proved

THE FUTURE PATTERN OF MEDICAL CARE

The future pattern of medical care is thus seen to emerge out of sheer scientific and social necessity *Hospital beds*, including the ancillary facilities which serve them, were planned during the war period in lavish quantity while the older influences were still at work, as a boon to the postwar era, but *have become excessively expensive to build and to maintain, far more expensive than the kind of community housing which can do so much to ease the burden of the hospital* Moreover, though this is the rock on which any hospital should be built, individualization of management is almost unattainable in the environment of the hospital ward to the same extent that it can be attained in the patient's home As a result, the patient remains a stranger among strangers, identified too often as a bed-number, with all of the psychosomatic consequences which this entails

For these reasons we are beginning to look to his home, or to the equivalent of his home, for the care of the patient, short-term or long-term, who does not require a hospital bed and for whom care at home is possible and preferable The formula emerges as follows *The care of the acute (short-term) and the care of the chronic (long-term) should be integrated in the general hospital on a continuing basis as long as the need for a hospital bed can be proved, the care of all others should be provided in their homes, or in the equivalent of their homes, by an extramural hospital program equal in service to the intramural hospital program* Under such a plan the bed in the patient's home comes as much under the protection of the hospital during illness as the intramural bed within the hospital—either independently, for the poor, or by a partnership of the hospital with the practitioner The location of the bed, intramural or extramural (with a

free interchange of patients between the two, is required) depends on the relation of two factors to each other, namely, (*a*) distance and (*b*) urgency. It is the degree of urgency, for example, which determines whether a shocked or exsanguinated patient shall remain on the operating table or be transferred to a recovery room located in the operating suite alongside. It is the degree of urgency which determines whether he can be moved to another bed on the same floor, a different floor, another pavilion, across the street, or into his home. Under this plan of hospital extension, the distance of the patient from the central therapeutic facilities of the hospital shows an inverse ratio to the urgency of his condition—the greater the urgency, the less the distance—provided that medical care is made to radiate from the hospital with easy elasticity.

The popularization of the hospital bed, which we have witnessed in the last few decades, has been converting the hospital into a court of first resort and has proved to be an expensive bit of propaganda which had the effect of closing the eyes of the public to the qualities of the home in relation to the hospital. The sulfa drugs (and chemotherapy in general), the antibiotic drug preparations (both of which are putting an end to the infectious diseases), blood and its fractions in shock and in hemorrhage, improved surgical technics and early ambulation, have had the effect of lessening the average stay of patients in hospitals and beds are now available for more intensive use, through better turnover, than ever before. As a result, we can now reduce the emphasis on the construction of additional hospital beds and transfer some of it to the patient's home, including beds in that location within the activities of the hospital. Hospital capacity and this means hospital census can be enlarged in this way at relatively small expense. The modernization of existing hospital facilities is, of course, in order, as well as the addition of beds, and the facilities which serve the e beds in locations where this is necessary.

It has been proved by successful experiment that a hospital can serve the patient in his home* (or in the equivalent of his home as, for example, in an institutional home in or near the hospital compound) at one-quarter of the cost to the community of serving him in a hospital bed. Any hospital can determine, through the joint efforts of physician and social worker, whether the home is suitable for extramural hospital service and plan for the patient that way, or recommend a home equivalent. *Total hospital bed capacity can be stated inclusively where an extramural program is integrated with an intra-mural program on a continuing basis.*

* See "Home Care—An Extra-Mural Hospital Function," in the Service Mal Monthly, April 1945, by the author (and the private pub) Bed Fact Are al Rep rt "The Dispute Cost of Home Care Me ter ie Hospital, New York City," by Dr. Marti (Serenity

since all beds are equally under identical hospital management This holds too for a medical educational and research program since extra-mural patients appreciate, equally with the intra-mural patient, the kind of consulting service which students can stimulate A combined service like this does, indeed, yield the best kind of teaching material for doctor and social worker alike It permits the practice of the new and advancing specialty of social medicine at its best Taking every advantage, and making use of every opportunity to further the social and medical interests of the patient, a quality of medicine is practiced in this way under the best auspices, leading to cure and then rehabilitation wherever these are attainable through human effort

This new pattern of medical care does away forever with distinctions which depend on age, social condition, address, and, above all, duration of illness It provides hospital beds, on a selective basis, to all those who need such major medical efforts as (*a*) a diagnostic work-up (*b*) major surgery (*c*) radiotherapy and (*d*) all other forms of intensive therapy which cannot be moved on wheels conveniently and inexpensively from hospital to home, and disregards the restraining criteria which have been governing the admission policies of acute general hospitals Those who do not need hospital beds are transferred under hospital care at home, or in the equivalent of the home, with the guarantee that hospitalization will again be provided, on a priority basis, in case of need Exactly the same staff serves both groups of patients and this service is therefore continuous The medical record, which remains a unit throughout both phases of medical care, may be brought forward in proof of this point *No one ever looks longingly to a hospital bed or, having experienced its discomforts, thinks of it nostalgically* Only for the most compelling reasons should a patient be weaned away from his home and brought to the hospital, apart from the cost involved in his transfer to such expensive facilities

THE HOSPITAL OF THE FUTURE

One can visualize such a comprehensive functional program on a continuing basis in simple structural terms Centrally located (in the community as well as in the group) is the heart of the enterprise, a vertical stack of architectural elements in which are concentrated all of the diagnostic and therapeutic facilities, surrounded by or contiguous to an adequate number of "acute" beds which depend on immediate juxtaposition Radiating from this central structure and varying in location, proportion, combination and correlation, are (*a*) the Department for Continued Care, where the long-term patient may be housed, (*b*) the private and semiprivate sections, (*c*) the outpatient department, (*d*) the tuberculosis service, (*e*) the department of neuropsychiatry, (*f*)

the group practice unit (including space for the department of home care), (*g*) the doctors' office building (there is no adequate *substitute for full time service in the top clinical positions in hospitals and in the junior positions which serve the home-care program*), (*h*) the rehabilitation center (including a sheltered workshop), (*i*) the convalescent unit, *and* (*j*) *the department of preventive medicine (health center)* The best service at the least cost to the largest number of people is possible in this set up *It avoids expensive duplication of hospital installations since central facilities are immediately available to all as needed*

Those who can afford fees for service are provided for in this plan of organization since they can pay *doctors of their choice in the hospital compound* Those who cannot afford fees are *provided for in the out-patient department* and those who are enrolled in group insurance plans have the group practice unit at their disposal For all classes, *hospital rooms*, wards and home service are available *The proportion of activities* enumerated here must naturally depend on circumstances in the community which they serve *The availability* of existing *buildings, the* economic status of the community, its housing facilities, *its health* and medical problems—all of these will influence the planners In any case, it must be emphasized here that *structural without functional integration will defeat the purpose of the project*

REHABILITATION AS THE FINAL GOAL

It goes without saying that the modern concept *of rehabilitation*, which projects the patient's cure into the *field of social* service where he can have the benefit of the next step in restoring him to complete or partial usefulness *in the community*, is *best applied in the integrated* plan here outlined For this purpose *occupational* therapy, coupled with the various modalities of physical medicine, are employed—what Rusk aptly *describes* as "dynamic therapeutics" This is done by a combined medical and social prescription which is written out in detail with the help of the specialist on the subject *and applied* either on the wards in the classrooms in the *home, or in* the sheltered *workshop In* this way prevention clinches the cure for we know that relapses are far less common where the patient is *restored* to economic usefulness under a sheltered medical and nursing program

The integrated plan of comprehensive care bring doctor and social worker together at last and both are dedicated to the task of caring for the sick and the near sick wherever they may be no matter what illness they may be suffering from, *or for* how long with the goal of restoration always in mind They can have no more worthy cause for their joint effort and require only the partnership of the philanthropist and the public servant to achieve success

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From the Massachusetts General Hospital, Boston

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CORRECTION

The Gay Clinic of Biloxi, Mississippi informs us that the prescription quoted in the footnote, page 420, of the March 1949 number of this publication is not representative of their procedures in the treatment of asthma Furthermore they advise that using the quantity of the different ingredients in the proportion quoted could be harmful to some patients as many patients are sensitive to these drugs in the amount advocated and might be expected to react violently A thorough study of each patient must be made to properly evaluate his requirements

THE MEDICAL CLINICS
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SYMPOSIUM ON RECENT ADVANCES IN MEDICINE

TREATMENT OF TOXIC GOITERS WITH RADIOACTIVE IODINE

EARLE M. CHAPMAN, M.D. AND ROBLEY D. EVANS, PH.D.

The idea of treating diseased tissues by means of radioactive substances was probably developed in a consultation between a physicist and a physician. Professor Henri Becquerel of Paris carried a small vial of radium in his vest pocket to a lecture in London in 1901, a few weeks later he noticed a reaction on the skin of his abdomen and this led him to visit his friend and physician Dr. Ernest Besnier. At this consultation it was recognized that the rays from radium can injure normal tissue and therefore they might be used to destroy diseased tissue.

Physicists and physicians again combined to start a new era in the use of radioactive substances in the treatment of diseases. Radioactive iodine had been produced by Fermi in 1934, but in 1936 Karl T. Compton and Robley D. Evans of the Massachusetts Institute of Technology brought this to the attention of physicians.

Earlier publications[1, 2, 3, 4] have reviewed the preliminary investigations and use of radioactive iodine as both a diagnostic and therapeutic aid in thyroid disorders. In brief, the specific affinity of the thyroid for iodine has been utilized, iodine tagged with radioactivity can be traced to the thyroid and its degree of affinity measured. The thyroid that traps a larger than normal

From the Thyroid Clinic of the Massachusetts General Hospital and the Radiation Laboratory of Nuclear Science and Engineering of the Massachusetts Institute of Technology, Boston.

amount is considered to be hyperplastic· such a gland can easily retain enough radioactivity to destroy itself

This highly selective form of tissue radiation depends on the specific nature of radioactive isotopes The bombarded atom by capturing a neutron has become an unstable nucleus which achieves its stability only by emitting an electron. I^{131} (radioactive iodine that emits one-half its electrons in eight days) sends out two kinds of rays, beta and gamma. The beta rays, which are high speed electrons, penetrate to a circumference of about 8 mm and act the same as the high speed secondary electrons of x-ray to destroy tissue The gamma rays have little tissue effect, but carry a distance of about 1 meter and so are easily detected by the Geiger counter.

TABLE 1

RESULTS IN SIXTY-FIVE PATIENTS GIVEN I^{130} (TWELVE-HOUR RADIOACTIVE IODINE), 1943–1946

Average estimated thyroid weight	45 gm
Average single effective dose by mouth	32 millicuries (14–79)
Average single effective dose retained per gram thyroid	0 45 millicurie/gm
Radiation sickness	6
97 per cent of radiation delivered in approximately	3 days
Given second doses	15*
Average interval to normal basal metabolism rate	1 month
Responded and continue well	50
Resulting hypothyroidism	11
Better, but toxic 6 months after treatment	3
Died	1
Recurrence of disease	0

* Five of these received I^{131} for their second dose, the other ten received I^{130}

During the past six years we have used radioactive iodine as a single therapeutic agent for 200 patients with toxic goiters, both diffuse and nodular The results of this treatment are the chief purpose of this communication

Between March 1943 and January 1947 we treated sixty-five patients with diffusely hyperplastic thyroids with the isotope I^{130}, which has a half life of only twelve hours This was produced on the cyclotron at the Massachusetts Institute of Technology The results in these sixty-five patients are depicted in Table 1. Sixty-four patients continue under observation in the Thyroid Clinic and all have had shrinkage or disappearance of the goiter and they appear fit and satisfied with the state of their health One woman died five years after such treatment from carcinoma

of the right bronchus with multiple metastases At autopsy her thyroid weighed 11 gm and was diffusely fibrotic and contained a tiny metastatic area of squamous cell carcinoma

The doses employed in the last twenty-seven of these patients treated with this twelve-hour isotope are shown in Table 2 The toxic effects of this short-lived form of radioactivity were nausea, slight fever, and swelling and tenderness of the thyroid for one or two days after the treatment Histologic examination of the thyroids of four of these patients have been done one, two and five years after treatment According to more than one pathologist they show only fibrosis and regenerative hyperplasia

The United States Atomic Energy Commission released I^{131}, the isotope with a half life of eight days, for use in a few clinics in the summer of 1946 and from then until June 1949 we have treated an additional 135 patients with hyperplastic thyroids The doses, the several clinical features of the response to I^{131} and the subsequent health of these patients deserve detailed attention

TABLE 2

DOSES OF I^{132} (TWELVE HOUR RADIOACTIVE IODINE) RECEIVED BY TWENTY-SEVEN PATIENTS, MAY 1945–MAY 1946

Average dose by mouth	52 6 millicuries
Average dose retained	20 0 millicuries
Average dose retained millicuries/gram thyroid	0 45 millicuries

DOSAGE

The dosage of radioactive iodine is estimated on the basis of thyroid gland size, since it is obvious that the results derive from the interaction of two variables energy and mass Estimating that the normal thyroid approximates 20 gm in size we estimate the size of each goiter in the number times normal so that a 2X goiter equals 40 gm of tissue 3X = 60 gm, etc Beginning with doses by mouth of about 0 10 millicuries per gram of estimated thyroid weight we discovered that five of the seven were inadequately treated and required second doses Thus the dose was gradually raised upward until with doses of 0 20 millicuries/gram we found evidence of overtreatment in the early appearance of myxedema The proper dose being thus bracketed we then lowered the estimated ideal dose to 0 16 m c/gm To the average patient we now give total doses of 6 to 10 millicuries in a single drink like water Our largest single dose for hyperthyroidism has been 1[illegible] millicuries

In fifty-one patients who have responsed to a normal thyroid state after treatment with a single dose we later found that the retained dose (actual dose less amount excreted in the urine in forty-eight hours) averaged 0 11 mc /gm Another way to express this is that the average urinary loss was 31 per cent of the ingested dose

In the eight patients who were overtreated and became myxedematous the retained dosage was found to average 0 13 mc /gm Possibly this figure should be greater as a large error may lie in overestimating the gland size and so overtreating them A better estimation of the therapeutic dosage can be made for each patient by determining the thyroidal collection of a tracer dose of I^{131} before therapy We found that in forty cases the tracer dose total urinary excretion in forty-eight hours averaged 29 per cent and the succeeding therapeutic dose excretion averaged 28 7 per cent With such close correlation it is evident that one could predict the amount that would be retained and so better estimate the dose required to render the patient euthyroid The use of tracer doses in this manner requires the technical aide and physical equipment to obtain rapid determinations The same index of function can be obtained by Geiger counting of the collection of radioactivity by the thyroid forty-eight hours after a tracer dose Data on the correlation of urinary excretion and thyroid collection of the same tracer dose has been collected by Skanse.[15]

CHOICE OF PATIENTS

The choice of patients was, for a time, limited to persons over forty-five years of age, but during the past year we have not made any restrictions because of age In the clinic approximately one-third of the new patients are treated by operation, one-third by prolonged drug therapy and the other third given radioactive iodine provided that they agree to a gland biopsy at some future time Twenty-five per cent of the patients given radioiodine had previous subtotal thyroidectomies for this disease It is of some interest that their disease had recurred from one to thirty years after operation Other reasons for the choice of internal radiation therapy were the probability of poor operative risk and the presence of severe eye signs No clear indications against radioiodine therapy are known Renal damage and congestive cardiac failure are known to delay the excretion of radioiodine

The diffusely hyperplastic gland responds much better than does the nodular gland, but this may be determined before treat-

ment by the use of tracer studies. Unless the nodular gland is avid for iodine there is no expectation of success unless one gives many doses. The occasional nodule that is hyperfunctioning may retain enough radioactivity to make treatment effective, but this can be determined only by directional counting after a tracer dose of I^{131}. In this series only six patients with nodular goiters were treated and four of these responded to a single dose.

The occasional pregnant woman who is thyrotoxic presents a problem in care, one that has recently been reviewed by Haines.[8] We found[9] that the fetal thyroid does not begin to collect radioiodine until the fourteenth week. It has been found safe to treat thyrotoxic women with radioactive iodine up to the fourth month of pregnancy. Two patients so treated have been delivered of healthy children who are developing normally.

RESPONSE TO TREATMENT

The response to radioactive iodine is characterized by a gradual return to a state of normal thyroid function over a period of six to twelve weeks. Individuals vary considerably in their response, but the average interval before a normal metabolic rate is attained is close to two months. Although 97 per cent of the radiation is delivered within the thyroid in a period of thirty days, the physiologic effect consequent to fibrosis and loss of gland structure goes on for several weeks. An index of this is the fact that the myxedema which appeared in eight patients was definitely established in twelve to twenty weeks (average sixteen) after treatment. One patient (Fig. 229) had a progressive decline in her metabolic rate until the third year after treatment when she was judged myxedematous. In these individuals the goiter disappeared and no thyroid tissue could be palpated. In those with large goiters (4 to X) who responded to radioactive iodine, the gland usually became hard or firm and about twice normal in size.

Response to treatment also included a slowing of the heart and often a restoration of normal heart rhythm. The decreased demand on the heart was followed in many instances by the clearing of the symptoms and signs of congestive heart failure. Indeed this aspect of the response to radioiodine is so impressive that we are preparing a separate report of the effects on the cardiovascular system. A decrease in the blood level of protein bound iodine (thyroid hormone) and usually an favorable improvement in the eyes were observed in the weeks subsequent to treatment. These changes are gratifying to the patient. Although the disappearance of fad

spasm, lid retraction, edema and chemosis may be evident, the measureable change in exophthalmos may be insignificant The ophthalmopathy of Graves' disease is still one of the most baffling problems in medicine The chief reason for this is our ignorance of its cause There are many theories, but there is no clear proof of the cause of the bulging, staring eyes, which may be associated either with an elevated or a normal metabolic rate Fourteen of these 200 patients had severe eye signs with hyperthyroidism We have learned that the eyes of these patients usually improve

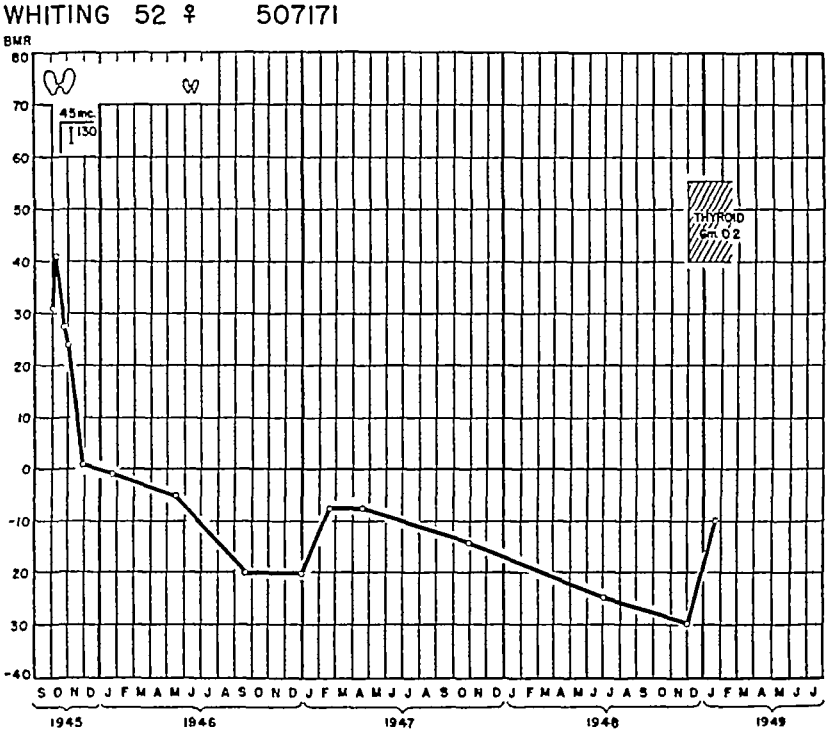

Fig 229 Metabolic rates in a patient treated with radioactive iodine

after radioiodine therapy None of them have become worse, an unfortunate sequel occasionally seen after subtotal thyroidectomy The photograph published in our original paper showed the marked changes, especially the loss of lid spasm and retraction after treatment Exophalmometer measurements before and after treatment indicate that the degree of exophthalmos changes very little and that the appearance of improvement results chiefly from loss of chemosis, lid retraction, and edema

Whether this effect on the eyes is a result of the reaction of

radioiodine on the thyroid alone or at some other physiologic or anatomic level, is unknown. The fact that iodine is known to occur in the pituitary leads to a reasonable suspicion that some reaction occurs in this organ, especially in the anterior or middle lobes. Indeed, Sturm[7] is inclined to believe that the anterior pituitary is the controlling center of iodine metabolism. We are now engaged in studying the uptake of radioiodine by the human pituitary. Closs[8] has confirmed Wells' early observations[9] and shown that fresh mammalian anterior pituitary contains 80 to 100 gamma per cent total iodine. Sturm and Buchholz[10] found that fresh human whole pituitaries contained about 80 gamma per cent iodine. According to Koppenhöfer[11] the posterior lobe of the pituitary is low in iodine, a fact that coincides with the observation that histologic changes occur only in the anterior and middle lobes after thyroidectomy. Likewise, Elmer[12] reviews the experimental data indicating that removal of the pituitary is associated with an increase in blood and urinary iodine.

There has been a hope that the response to radioiodine might be augmented by techniques that would either hold the radioactivity in the thyroid or increase the uptake by the thyroid. Hertz[1] concluded that it was important to give iodine, the reason presumably being that it would add the ordinary iodine response to the clinical course of the disease. We found[4] in seven patients with hyperthyroidism given both I^{131} and potassium iodide that the curves of basal metabolic rate fell in a manner identical to those who received only the radioactive iodine and that the clinical response seemed identical. Then Freedberg and Buka[13] found that the addition of iodine twenty-four hours after a dose of I^{131} markedly increased the urinary excretion of radioiodine and caused a pronounced fall in thyroid radioactivity. The administration of stable iodine beginning three days after I^{131} dosage was accompanied by only a small increase in urinary excretion of radioactivity and no change in counts over the gland. In order to test this we measured the daily urinary excretion for a prolonged period after a therapeutic dose of I^{131} and found that the addition of potassium iodide on the third and fifth day was followed by a measurable increase in the urinary content of radioactivity (Table 9).

Although it is well known that iodine in several forms will interfere with the collection of radioiodine by the thyroid, it has not been determined how long iodine must be omitted before the thyroid again becomes avid for the radioiodine. It has been recommended that therapeutic doses of I^{131} should not be given for at least

one month after the omission of stable iodine in order to allow maximum uptake of radioactive iodine Although we might apply the iodine response and relapse curves of the basal metabolic rate and assume that the gland becomes avid for iodine twelve to fourteen days after omission of iodine, we decided to test this point (Table 4) These data indicate that effective therapeutic doses of radioiodine may be given as early as twelve days after the omis-

TABLE 3

PER CENT I^{131} IN URINARY EXCRETION POTASSIUM IODIDE ADDED ON SIXTH DAY IN FIRST CASE AND FIFTH DAY IN SECOND

	Hours			Days							
	0–6	6–12	12–24	2	3	4	5	6	7	8	9
Stevenson	12 0	1 3	1 6	3 5	1 8	2 0	1 8	2 6	2 7	2 5	2 6
Knight	16 6	7 2	3 6	2 4		0 5	1 5	1 7	0 8		

TABLE 4

RESPONSE TO RADIOIODINE IN RELATION TO LENGTH OF PERIOD AFTER OMISSION OF STABLE IODINE

	Days Off Iodine Therapy	Therapy Dose I^{131}	Per cent of Urinary Excretion Radioactivity		
			0–24 Hr	24–48 Hr	Total 48 Hr
Balboni 28136	12	13 mc	7 5	3 0	10 5
Donna 633439	16	5 mc	11 5	1 3	12 8
Munroe 359934	23	11 mc	15 0	3 6	18 6
Mangiaracine 42039	24	8 mc.	24 9	2 5	27 4

sion of stable iodine, and thus there is no need to keep a thyrotoxic patient free of other forms of treatment for longer periods before radioiodine therapy

Next we considered the possibility that the avidity of the thyroid for radioiodine could be increased by preparation with a thiouracil drug The plan followed with Skanse[15] in eight cases of hyperthyroidism was as follows

1 Tracer dose I^{131}

2 Propylthiouracil 300 mg daily for fourteen days
3 Tracer dose I^{131} on fourteenth day
4 Propylthiouracil omitted on sixteenth day
5 Tracer dose I^{131} on eighteenth day
6 Therapy dose I^{131} on twentieth day

The data from Table 5 clearly indicate that propylthiouracil partially blocks the collection of radioiodine by the thyroid and that by the second and fourth day after omission of the drug there

TABLE 5

STUDIES ON I^{131} URINARY EXCRETION—BEFORE, DURING AND AFTER PROPYLTHIOURACIL IN PATIENTS WITH HYPERTHYROIDISM

	Tracer Doses I^{131}						Therapy Dose I^{131} 96 Hr after Treatment	
	Before Treatment		During Treatment		48 Hr after Treatment			
	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr
1 Green 501794	27	1 7	62 6	7 9	25 4	1 8	25 6	2 2
2 Wood 556905	21 6	3 1	65 8	10 9	23 7	6 2	27 7	4 4
3 Ciolli 601501	32 6 32 0	2 5 2 7	35 3	5 9			31 9	31 9 1 9*
4 Hynes 582170	21 6	2 5	33 3	3 6	18 6	5 2	16	1 4
5 Elliott 406037	10 3	2 1	26	4 4	4 9	1 2	6 6	1 2
6 Elster 471232	21 1	0 4	22 0	0 4	49 1	10 5	29 5	1 0
7 Camire 559770	3 3	1 8	25 6	7 1	5 3	2 3	4 5	1 6
8 Lang 601233	0 0	1 0			15 [illegible]	3 0	0 1	2 0

* Forty-eight hours after propylthiouracil was stopped

is no appreciable increase in avidity above that before the treatment was started The excretion of radioactivity was usually greater the third day than the fifth day after propylthiouracil was stopped These observations suggest that patients with hyperthyroidism who have had their symptoms controlled or their disease ameliorated by propylthiouracil should omit the thiouracil drug for four days before treatment with radioiodine

Table 6 gives the results in 186 patients with hyperthyroidism treated only with radioiodine over a three year period

One of the most important observations made on the response to treatment has been the microscopic study of these irradiated tissues To date we have reviewed tissue from seven patients who had received radioiodine from nineteen days to five and one-half years prior to the anatomic study The tissue removed nineteen days after treatment showed evidence of acute cellular injury with cellular swelling and apparent loosening of the follicle cells from the basement membrane, fibrosis was not observed until tissue was removed five months after therapy Fibrosis and regenerative hyperplasia commonly appeared in tissue removed one, two and five years after radiation One patient died five and one-half years after treatment because of carcinoma of the right upper bronchus with metatastases to the cervical, supraclavicular, axillary, bronchial, mediastinal, porta hepatis, retroperitoneal and inguinal lymph nodes, likewise colonies of tumor were found in the

TABLE 6

RESULTS IN 135 PATIENTS WITH HYPERTHYROIDISM TREATED ONLY WITH RADIOIODINE, AUGUST, 1946—JUNE, 1949

Responded and continue well, 1 dose	104
2 doses	11
Better but toxic six months later	8
Died, myocardial infarction	1
Treated within three months	10
Operated	1

right lung, liver, both adrenals, kidneys, the pancreas and terminal ileum The right lobe of the thyroid harbored a tiny (2 mm) area of metastatic squamous cell carcinoma, the gland as a whole was firm, fibrotic and weighed 11 gm and had the appearance of fibrosis encircling distorted follicles that contained cells of above average in mean cell height (see Fig 230)

It is our plan to obtain more biopsies from patients as the years elapse. By following a small, select group for a twenty-year period we should be able to answer definitely the question of the hazard of this treatment being carcinogenic

In discussing the quantitative aspects of radiation carcinogenesis in humans, Evans[14] found that the doses required to produce osteogenic sarcoma by chronic radium poisoning, lung carcinoma from breathing radon, liver sarcoma following thorotrast and skin carcinoma following exposure to gamma rays have the following factors in common

1 A delay of ten to twenty years between the beginning of radiation and the recognition of malignancy
2 A low level radiation dose maintained over a period of many years

From this comparative analysis it seems extremely unlikely that radioactive iodine therapy that releases 97 per cent of its energy into the tissues in thirty days will induce carcinoma in the thyroid or urinary excretory passages

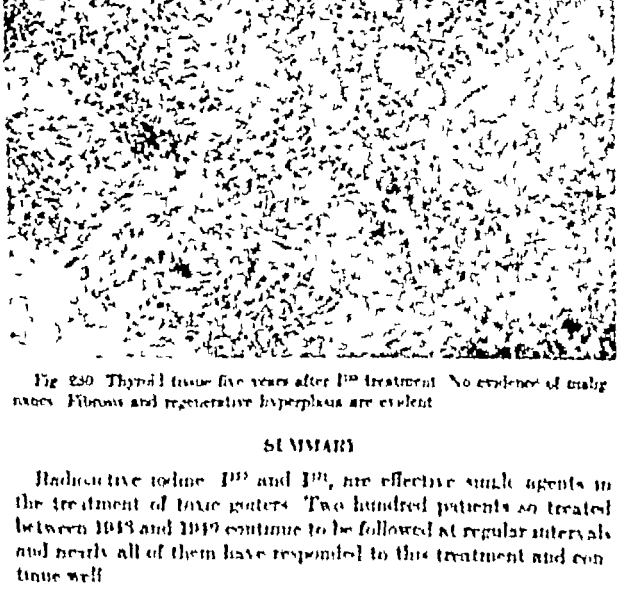

Fig 230 Thyroid tissue five years after I^{131} treatment No evidence of malignancy Fibrosis and regenerative hyperplasia are evident

SUMMARY

Radioactive iodine I^{132} and I^{131}, are effective simple agents in the treatment of toxic goiters Two hundred patients so treated between 1943 and 1949 continue to be followed at regular intervals and nearly all of them have responded to this treatment and continue well

No clear indications against the use of radioiodine are known although we advise against its use beyond the fourth month of pregnancy

The method of internal radiation therapy has been particularly helpful in the recondite patient who has often received the least to

normal function Patients with severe eye signs have been greatly benefited

Patients with hyperthyroidism who are taking iodine should omit such treatment at least twelve days before receiving radioactive iodine, those taking thiouracil should omit the drug four days before receiving radioiodine In our experience there is rarely a need to give antithyroid drugs subsequent to radioiodine therapy

After eight years of this treatment and after histologic study of thyroid tissue removed from nineteen days to five and one-half years after the administration of radioactive iodine, there is no evidence that these therapeutic doses are carcinogenic

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THYROID NODULES, BENIGN AND MALIGNANT, OBSERVATIONS ON THEIR FUNCTION

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For many years the function of thyroid nodules was usually assessed by their appearance under the microscope When radioactive iodine was made available as a tool for studying thyroid tissue, it became possible to interpret function in terms of the gland's capacity to collect this isotope [1 2 3 4] It was soon evident that hyperactive thyroid tissue, as in Graves' disease, collected much more radioactive iodine than the normal gland The following observations have been made on the assumption that the ability to collect radioiodine is a measure of the biologic activity of thyroid tissue

Radioautographs are images produced by the exposure of photographic film to tissue containing a radioactive substance Since the degree of blackening on the film is proportionate to the concentration of radioiodine in the tissue, this affords an opportunity to observe the relative function of thyroid nodules [4] Such a radioautographic study has been in progress for the past two and one-half years at the Thyroid Clinic of the Massachusetts General Hospital and observations have been made on almost all cases of nodular goiter upon which thyroidectomy was performed

A standard tracer dose of radioiodine was given to the patient twenty four to forty-eight hours before operation so that the radioiodine might become fixed in the thyroid Blocks of tissue composed of both the nodule and the extranodular thyroid tissue were cut from the excised gland Microscopic sections composed of both types of tissue were exposed to photographic film by direct contact When the film was removed and developed, the areas of blackening corresponded to the location of the radioactive iodine in these tissue sections Such preparations were made from most of the nodules removed from over 200 patients with nodular goiter

Special attention was directed toward those completely encapsulated, discrete tissue masses the histologic pattern of which was different from the remaining thyroid When all of these discrete encapsulated nodules were arranged in a spectrum beginning with

From the Thyroid Clinic and the Department of Surgery of the Harvard Medical School, the Massachusetts General Hospital, Boston
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the least differentiated or most embryonal and progressing to the more differentiated types, it was found that, in general, the degree of differentiation of the nodule ran parallel to the degree of function as measured by the uptake of radioactive iodine The stages in the embryonic development of the thyroid will be used to illustrate the types of differentiation seen in these nodules, but it should not be inferred that such a sequence necessarily takes place in the growth of a nodule

Beginning at the undifferentiated end of such a spectrum, the solid cellular nodules which are composed of sheets of cells without acini are comparable to the earliest stage of embryonic development and they have no demonstrable uptake of radioactive iodine According to Norris,[5] the next stage of embryonic development is that of solid masses of cells arranged in strands without acini Nodules with this pattern were called struma nodosa trabecularis by Wegelin[6] and in this study they also were found to have no avidity for radioactive iodine Nodules which resemble the next stage of embryonic development are those with strands of cells containing minute cavitations suggesting tubules These were called struma nodosa tubularis by Wegelin [6] Radioautographs show that lesions with this histologic pattern take up only very minute quantities of radioactive iodine In embryonic development these tubules apparently give rise to minute acini which gradually acquire colloid Nodules showing this pattern and called struma nodosa microfollicularis by Wegelin[6] have increasing amounts of radioiodine uptake corresponding with the appearance of the colloid It has been shown by Chapman and his associates[7] that at about this stage in embryonic development the human fetus begins to collect radioactive iodine Nodules which were composed of mature acini displayed more active function At this more differentiated end of the *spectrum* there were two exceptions to the parallelism between differentiation and function One of these was the so-called colloid nodule which was composed of large acini, distended with colloid and surrounded by flat epithelium This type of nodule had a relatively meager uptake of radioactive iodine and might be interpreted as being due to a resting or "overripe" stage The other exception to this parallelism was a group of well differentiated hyperplastic nodules with little or no function Particular attention will be directed toward discussing these later

Investigators have had difficulty in correlating cellular hypertrophy and hyperplasia of nodules with clinical thyrotoxicosis [8, 9] Hyperplastic nodules have been found in patients with clinical

thyrotoxicosis, but such nodules have also been found in patients who were not thyrotoxic. From an analysis of the autoradiographs of the hyperplastic nodules with cellular hypertrophy in this series, it was apparent that while many collected much higher concentrations of radioactive iodine than the remaining thyroid, others collected less than the extranodular tissue, or even none at all. The cellular hypertrophy was confirmed by measuring the cell height of 100 cells (one average cell in each of 100 acini) and finding a mean cell height greater than in the extranodular thyroid. Further analysis of these data showed that those nodules which were functioning excessively were composed of cells whose height, in general, was rather uniformly increased, whereas those hyperplastic nodules with cellular hypertrophy which showed little or no function were composed of cells with a tendency toward more variation in height. Although the mean cell height of the less active nodules was increased, many individual cells were considerably lower and others considerably *higher than this mean. This offers one reason why it* is possible to have a patient without thyrotoxicosis but with a hyperplastic lesion with cellular hypertrophy, namely, some of these lesions do not function.

Among the large group of hyperplastic nodules there were some which had so much cellular hypertrophy and hyperplasia that it was difficult to draw the distinction between benign hyperplasia and true malignant papillary adenocarcinoma. When all of the hyperplastic nodules with little or no function were grouped together, examples with more and more hyperplasia and more and more variation in cell height appeared to merge into frank papillary adenocarcinoma. Whether these hyperplastic nonfunctioning nodules belong to the same family as the papillary adenocarcinomas, *which are also functionless, remains to be decided.*

An analysis of the hyperfunctioning nodules, i.e. hyperplastic nodules with cellular hypertrophy and relatively more function per unit area than the extranodular thyroid, revealed that these lesions occurred in patients with or without thyrotoxicosis. Although the basal metabolism in some cases was definitely elevated and there were clinical signs of thyrotoxicosis, there were other whose basal metabolism ranged as low as minus 10. In those cases with [illegible] that toxic [illegible] was found that the nodule was either so small or so extensively necrotic that the total functioning cell [illegible] was in all event to correspond to the large amount of thyroid hormone. The theory might be advanced that such hyperfunctioning nodules [illegible] would [illegible]

and eventually produce thyrotoxicosis Such a theory might be supported by Plummer's observation[10] that an average of 17 6 years elapsed between the discovery of a nodule and the onset of the toxic symptoms which prompted the patient to seek medical advice

We have seen patients who had a nodular goiter with thyrotoxicosis, or who had a clinical history of it who lost their thyrotoxic symptoms spontaneously over a period of several months When the patient finally agreed to have the nodule removed, it was found to have undergone recent necrosis in the center, however, the radioautograph revealed that just within the capsule were a few viable cells which were functioning excessively It would seem that such a patient had experienced at least a temporary remission due to the spontaneous necrosis in a nodule whose total functioning cell mass had originally been sufficient to produce thyrotoxicosis It is especially interesting that the nodules with hyperfunction were the ones most frequently found to have central necrosis

When the mean cell height of the hyperfunctioning nodule was compared to the mean cell height of the remaining thyroid and also related to the autoradiographic findings, some interesting correlations were found In patients with a definitely elevated basal metabolic rate, the mean cell height of the remaining thyroid was usually clearly below that of normal Coincident with this depression in cell height there was a decreased or absent function in this same remaining thyroid tissue In patients with hyperfunctioning nodules in whom elevation of metabolism had not occurred, the depression of mean cell height and of function was usually not so striking All degrees of this suppression of the remaining thyroid were observed in the group of cases studied These findings direct attention to that group of patients with nodular goiter who do not show a demonstrable elevation in metabolism, but nevertheless complain of mild symptoms of thyrotoxicosis or cardiac strain It is well known that some of these patients experience a surprising sense of well-being after the nodules are removed Radioautographs from such patients often reveal hyperactivity in the nodule These observations when associated with a temporary postoperative decline in basal metabolism suggest that the removal of the nodule was of more than psychological benefit

From the above observations it is now reasonable to propose some explanation for the presence of a hyperplastic nodule with cellular hypertrophy in the absence of thyrotoxicosis This situation may result from

1 Nodules showing hyperplasia and cellular hypertrophy but with no apparent capacity for function
2 Nodules showing hyperplasia, cellular hypertrophy and a relatively increased function, but a total functioning cell mass too small to cause symptoms
3 Nodules with hyperplasia, cellular hypertrophy and increased function, but with a major loss of the total functioning cell mass, the result of necrosis

Although many carcinomas of the thyroid have relatively little or no avidity for radioactive iodine, there are a few exceptions In our experience papillary adenocarcinoma of the thyroid practically never has an affinity for radioactive iodine Alveolar adenocarcinoma of the thyroid shows great variation in its affinity for radioactive iodine, occasionally taking up significant amounts These functioning alveolar adenocarcinomas often closely resemble normal thyroid tissue and some have been called "benign metastasizing strumas" For the most part, the highly malignant cellular types of carcinoma have no function, as might be expected from their degree of undifferentiation However, three tumors of this type have collected sufficient radioactive iodine to cause blackening on a photographic film

The members of the Thyroid Clinic of the Massachusetts General Hospital have been studying possible means of initiating or augmenting function in thyroid carcinomas After surgical removal of the entire thyroid gland it may be that the decline in the supply of thyroid hormone places a biologic demand on the remote metastases and thus induces a conversion to function By assay of biopsy material or by quantitative measure of the radioactivity over metastases it has been found that in a few cases these metastases have increased their capacity to collect radioactive iodine This working hypothesis has been explored with the hope that its understanding might be used in the radioactive iodine therapy of such metastases At the present time, any apparent benefit appears to arise in the retardation of growth in those less malignant lesions that resemble normal thyroid tissue Some observations indicate that the administration of thyrotropic hormones or thiouracil may be followed by an increased capacity of metastases to collect radioactive iodine If functional activity can be induced in metastases which are inaccessible to surgery, it may be possible to control their growth by the administration of radioactive iodine in therapeutic doses

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PROBLEMS IN THE DIAGNOSIS OF THYROTOXICOSIS

JOHN B STANBURY, M D

Few diseases in clinical medicine are so readily recognized as classic Graves' disease The prominent staring eyes, the goiter, the tense and anxious appearance, the tremor, the weight loss in spite of excellent appetite and the heat intolerance leave little doubt of the correct diagnosis Usually only a confirmatory determination of the basal metabolic rate is necessary before proceeding with treatment However, the diagnosis is not always so certain The ocular manifestations of Graves' disease may be simulated by myasthenia gravis The eyes may be congenitally prominent Orbital hemangiomas and leukemic infiltrations may cause prominence of the eyes The tremor, the anxious expression, the prominent bloodshot eyes, and the flushed face of the patient with incipient delirium tremens has led us to the use of the term "alcotoxicosis" in separating these patients from those with Graves' disease Some patients with severe hypertension have slight proptosis and stare

Graves' disease is to be distinguished from hyperfunctioning tumors of the thyroid The clinical picture may be quite obscure when there is absence of eye signs This is particularly true if the goiter is substernal, or if the excessive thyroid hormone is deriving from a single small nodule of hyperplastic tissue located deep in the neck and easily missed on routine physical examination Patients with anxiety states are oftentimes considered to be mildly thyrotoxic, while those with rheumatic heart disease with their drawn and anxious appearance, their weight loss and their cardiac irregularities may mimic the thyrocardiac very closely Profound muscle weakness and wasting may be a manifestation common to an overactive thyroid gland and myasthenia gravis

Until recent years the diagnosis of thyrotoxicosis was made from the clinical picture, the basal metabolic rate and at times the response to a therapeutic trial of iodine These methods are still fundamental and will doubtless continue to be so but there are now available two additional diagnostic aids of considerable help in equivocal cases These are the determination of the protein bound iodine, or "hormonal value" of the blood and the determi

From the Thyroid Clinic of the Massachusetts General Hospital Boston

nation of the urinary excretion of radioactive iodine Unfortunately, at the present time these require laboratory equipment and technical aid not generally available There are times when even these refinements may leave one in doubt as to the presence of thyroid disorder

RADIOACTIVE IODINE EXCRETION

The two most characteristic faculties of the thyroid gland are its ability to trap and hold the inorganic iodide of the blood, and its ability to convert this trapped iodide into a hormonally active protein complex which is secreted into the blood These two functions of the gland have been employed to measure the functional state of the gland One of these tests measures the avidity with which the gland traps a minute dose of radioactive iodine The second, to be described in the next section, measures the concentration of hormonally active material in the blood

If an exceedingly small quantity of radioactive iodine with an eight day half-life is ingested, the radioactivity can be detected quickly in the region of the thyroid gland with a Geiger-Müller counter The radioactivity in the gland builds up to a peak in twenty-four to forty-eight hours, and then slowly falls away as the iodine which has been formed into hormone is secreted into the blood and as the natural decay of the radioiodine progresses [1]

The quantity of a tracer dose of radioactive iodine excreted in the urine during the succeeding forty-eight hours serves as a good index of the avidity of the thyroid for iodine, and as such of the activity of the gland Thus, if little of the tracer material is excreted it can be assumed that most of it was trapped by the gland, and that the gland was hyperactive If less than 40 per cent is excreted in forty-eight hours the diagnosis of thyrotoxicosis is usually confirmed A certain amount of overlap has been found between the thyrotoxic and the normal patients and between the normals and the myxedematous, but in general this has become a useful and simple guide [2]

The following case illustrates the usefulness of the tracer technic in establishing a diagnosis

CASE I —Mr T , MGH No 619095, is a 71 year old man who was referred to this hospital because of weakness, weight loss and intermittent diarrhea for the past nine months He had lost a total of 56 pounds He had also been troubled by excessive thirst and frequency of urination For several months he had noticed a tremor of

his hands, but he insisted that he was not nervous Five weeks before admission he had a severe attack of abdominal cramps and diarrhea He felt hot and flushed at night, and on one occasion found his temperature to be 100 4° F He began to have palpitations in his chest

Except for evidence of weight loss the physical examination was not helpful There was no prominence of the eyes nor were there other eye signs of Graves' disease The thyroid gland was normal in size and consistency No bruit could be heard The heart was normal except for a pulse rate of 100 There was a perceptible fine tremor of both hands Routine laboratory examinations were normal His initial metabolic rate was plus 38 Another repeated a few days later was plus 51

In spite of the elevated basal metabolic rates, the history and the essentially negative physical examination diverted attention away from the thyroid Examination of the blood and stool disclosed no abnormalities A barium enema and an x ray of the chest were normal The patient was then given a tracer dose of radioactive iodine only 29 per cent of this was excreted during the next forty eight hours The diagnosis seemed no longer in doubt Consequently, he was started on 900 mg of propylthiouracil daily in divided doses The thyroid gland become more prominent and his metabolic rate fell to the normal range His symptoms disappeared and he gained 22 pounds At the present time he is asymptomatic. Since it was impossible to estimate the size of his thyroid accurately, or even approximately, and therefore impossible to estimate accurately the therapeutic dosage of radioactive iodine it was decided to continue the propylthiouracil for a six month period and then to discontinue it to see whether the disease recurs He continues under observation

The diagnosis in this patient was obscured by the absence of most of the usual physical signs of Graves' disease He had no eye signs and his thyroid felt quite normal in size and consistency. Increased activity of the gland as evidenced by its increased avidity for iodine was strong evidence in favor of thyrotoxicosis, and this was confirmed by the dramatic and satisfactory response to treatment This patient was a good example of the subtlety of thyrotoxicosis as it occurs in some males

PLASMA PROTEIN BOUND IODINE

After the iodinated dye of the plasma is taken up by the thyroid it is converted into thyroglobulin a complex protein containing a good deal of iodine and is secreted into the follicular colloid with the result that the iodine of the thyroid is bound to the pituitary this large molecule is broken down into a smaller component which is then

secreted into the blood as the effective product of the gland Thus, the hormonally active iodine of the blood is bound to protein and is derived from the thyroid Therefore, the determination of the protein-bound iodine content of the plasma is another index of the functional state of the gland The measurement and interpretation of this component of the plasma have been extensively explored and developed [3, 4, 5] The following patient illustrates the usefulness of this determination

CASE II —Mrs D , MGH No 563570, a 44 year old housewife, was treated medically for thyrotoxicosis when she was 20½ years old The diagnosis was made on the basis of a goiter, exertional dyspnea, prominence of the eyes, palpitations, and weight loss Iodine was given for a year Her symptoms disappeared and she was well for 23 years until about six months before the present admission, when the dyspnea, palpitations and an increase in appetite returned She lost 15 pounds She complained of weakness and thought that her eyes were becoming more prominent Six weeks before admission she began to take saturated solution of potassium iodide, 10 drops three times daily She felt better on this therapy

At the time of admission there was little evidence of thyroid hyperfunction The pulse rate was 76 and the blood pressure was normal The thyroid was about twice its normal size, the right lobe being larger than the left No pyramidal lobe was felt There were no skin changes There was neither lid lag nor prominence of the eyes The rest of the physical examination was negative The basal metabolic rate was minus 4 The cholesterol was 116 mg per 100 cc of plasma A second basal metabolic rate was plus 9 However, a determination of the protein-bound iodine of the blood was 10 2 gamma per 100 cc (normal 3 5 to 7 gamma per 100 cc) On the strength of the history, and particularly on the strength of the sharply elevated protein-bound iodine, a subtotal thyroidectomy was done Pathologic examination showed cellular hyperplasia of the thyroid She has been followed carefully in the Thyroid Clinic for the past two years She has remained symptom-free and has gained weight The basal metabolic rate has ranged between minus 20 and minus 28 Her skin has remained moist and fine, her voice has not become deeper, and her hair has remained the same She is alert and active In short, there is no clinical evidence of myxedema

The normal metabolism for this patient was 20 to 30 per cent lower than the average for a person of her height and weight This is not an infrequent occurrence since the calculation of the metabolic rate is referred to an average standard from which there are wide biological variations When she first came to the clinic

she had a metabolic rate 20 to 30 per cent above her own normal She had the signs and symptoms of toxicity also, but these were doubtless partially in abeyance from the medication with potassium iodide The elevated protein bound iodine was strong evidence in favor of an overactive gland The fall to metabolic rate levels of minus 20 to minus 28 with not the slightest evidence of myxedema supported the initial diagnosis and the treatment she received

LABORATORY TESTS NOT ALWAYS DIAGNOSTIC

One of the frequently encountered problems in a thyroid clinic is the patient, usually a young woman, who comes in because of nervousness, sweating and perhaps diarrhea and weight loss These patients may to all appearances have mild thyrotoxicosis, and this may seem especially true when they are first interviewed If, in addition, a slight enlargement of the thyroid is present, as is the case in many young women one may be easily misled The following case serves to illustrate the difficulty in clearly defining the role of the thyroid in a patient with anxiety symptoms

Case III —Mrs S, MGH No 60-19- an intelligent young woman of 40 had been well all her life except for a splenectomy for purpura several years earlier For a year she had been nervous and irritable and very easily fatigued About six months before first coming to this hospital she saw her family physician because of palpitations and shortness of breath on exertion He gave her iodine, but she did not seem to be helped by this medication Indeed her fatigue grew worse In spite of an excellent appetite she lost 25 pounds There had been no intolerance to heat The menses were quite normal

When the patient was first seen in this clinic she was described as a nervous emotional woman Her hair, skin and eyes were normal Her thyroid was palpable slightly enlarged and normal in consistency Her hands were moist and warm, and there was a fine tremor She had a barely detectable lid lag but otherwise the physical examination was normal Two determinations of the basal metabolic rate were plus 8 and plus 11 She excreted 8 4 per cent of a tracer dose of radioactive iodine in forty eight hours The protein bound iodine content of the blood was 8 8 gamma per 100 cc (normal 4 5 to 7) Because the diagnosis was in doubt she was given a drugs of [illegible] twice daily to see whether there might be a therapeutic response Subsequently, her basal metabolic rates were minus [illegible] Her pulse rate [illegible] but she had little or no change in her symptoms Because of the fall [illegible] the iodine test [illegible] she was given [illegible] by [illegible] was [illegible] for a [illegible] but she did not improve symptomatically She

continued to be nervous, apprehensive and very fatigued The only change noticed was that her thyroid increased somewhat in size and became firmer She was then admitted to the Surgical Service for thyroidectomy

At this time a more detailed history disclosed a severe personality and social problem When the patient was 3 years of age, her mother and father separated and her mother shortly thereafter committed suicide She was brought up by domineering foster parents As a child she had frequent night terrors and fear of the dark and other symptoms suggestive of neurosis She was married at age 18 to a chronic alcoholic, who after a few months became very abusive This culminated in divorce coincident with the beginning of the present symptoms She was married again shortly thereafter to a childhood acquaintance This marriage has been no happier than the first Her husband is a person with little understanding or tolerance of the patient's problems They have extremely limited finances

It seemed probable that many, if not all of the patient's symptoms arose from her conflicts and her limited capacity for adjusting to misfortune Accordingly, operation was cancelled and she was transferred to the Psychiatric Service for further study There, much additional data confirmed the presence of severe psychoneurosis She was finally discharged with a diagnosis of anxiety state She has subsequently been followed jointly in the Psychiatric and the Thyroid Out-Patient Clinic She has not improved symptomatically despite the continued use of iodine and intensive psychotherapy If anything, her home situation has deteriorated The last determination of her basal metabolic rate was minus 10 At that time her physical examination was essentially as described at the time of entry, except that the thyroid was a little larger and firmer The relative importance of the thyroid gland and of psychological and sociological factors in producing her symptoms is still undetermined

Much of the objective data obtained on this patient favored a diagnosis of thyroid hyperfunction The protein-bound iodine content of the blood and the radioactive iodine excretion were both suggestively elevated On the strength of these findings, in addition to the slightly enlarged thyroid and the minimal eye signs, the diagnosis of thyrotoxicosis was so seriously entertained that she very nearly underwent surgery It is unusual indeed for a patient with Graves' disease to fail to respond symptomatically to iodine therapy or to the goitrogenic drugs Usually a few days after beginning iodine therapy the thyrotoxic patient will volunteer that he is vastly improved, and the same thing is true over a longer time after treatment with thiouracil and its derivatives

This patient failed to obtain any relief from her dominant symp-

tom, fatigue, from either a thorough trial of iodinization or a prolonged period of propylthiouracil therapy. When an exceedingly difficult social and psychological situation was brought to light it seemed clear that it would be unwise to proceed with surgery. There was need for further consideration not only of the diagnosis, but of the plan of management. Certainly, after considerable study, it seemed that most if not all of her symptoms could be explained by her anxiety state, yet it was difficult to disregard the abnormal protein bound iodine and the radioiodine excretion. The result has been that we are still undecided whether the patient is thyrotoxic or not. We have decided, however, that thyroid disease, if present, is not of sufficient severity to cause great concern as such. There is no urgent necessity of proceeding with any form of definitive therapy. If she is thyrotoxic it is most probable that this will become overt in time. Meanwhile it seems most wise to continue to watch her and to do what can be done to readjust her deplorable home situation and to give her the psychiatric support which she so evidently needs.

The most disturbing thought about this patient is that a small component of thyrotoxicosis may be making manifest or accentuating an otherwise trivial or latent anxiety state. Emotional lability and fatigue are frequent symptoms of hyperthyroidism and psychoneuro is alike and the presence of the first may enhance the second, although patients with anxiety neurosis commonly show a normal or a subnormal metabolic rate. If we could be even reasonably sure that this patient had masked hyperthyroidism we would proceed with definitive therapy, such as surgery or radioactive iodine. Since reasonable doubt remains we have been forced to adopt a program of watchful waiting. We have been unwilling to accept as unequivocal evidence the protein bound iodine and the radioactive iodine determinations.

DIAGNOSIS ON CLINICAL GROUNDS ALONE

Infrequently occasions arise when none of the usual objective tests for thyroid disease are practicable. Then reliance must be placed solely on clinical judgment. The following is an illustrative case.

Case IV. M. P. McH. No. [illegible] [illegible]

months before admission she became to have pain in the epigastric region This was not related to the intake of food or to exertion, or to anything else She became short of breath, had palpitations on exertion, and lost about 60 pounds in weight She gave no history of an increase in appetite or of diarrhea On the contrary, she was constipated Five weeks before admission to this hospital, following a period of extreme breathlessness and smothering, she was admitted to another hospital There, because of the mass in her neck, many attempts were made to obtain a satisfactory basal metabolic rate, but none of these were successful None the less she was given propylthiouracil for several weeks This failed to relieve her exertional dyspnea or her palpitations

At the time of admission to this hospital the patient was extremely ill She was orthopneic, cyanotic and a little jaundiced Both eyes were slightly prominent, the left a little more than the right The thyroid was diffusely enlarged to twice the normal size It contained no nodules The blood pressure was 140 systolic and 90 diastolic The pulse at the apex was 160 and was grossly irregular At the wrist it was 140 No murmurs could be heard The apical impulse was felt in the anterior axillary line There was pitting edema below the knees A large tender mass in the right upper quadrant and in the epigastric region was thought to be a congested liver She was vomiting frequently The urine showed a trace of albumin and a small amount of bile There were many blood cells in the sediment The white blood cell count was 7200 and the hemoglobin was 12 0 gm per cent The blood smear was normal, and no occult blood was found in the stool

Considerable difficulty was encountered in adequate digitalization of the patient because of her vomiting She was given 1 6 mg of digitoxin, but probably retained only 0 8 mg She was then given 0 8 mg of cedilanid, but in spite of this after seventy-two hours her apical pulse rate was still 120 per minute and her heart was still fibrillating Following an intravenous mercurial diuretic she lost about 15 pounds in weight Because of the suggestive findings of slightly prominent eyes and enlarged thyroid she was seen in consultation by Dr Jacob Lerman He was able to demonstrate a definite lid lag, a globe lag and prominence of the eyes with puffiness of the eyelids It was his opinion that thyrotoxicosis was contributing materially to her rapid and uncontrolled fibrillation and to her heart failure

The patient was too ill to have a basal metabolic rate determination Assay of the protein-bound iodine content of the blood or of the radioactive iodine excretion would have taken too long a time to be of any value in the acute emergency that the patient presented Reliance, therefore, was placed solely on the clinical impression Because of her continued vomiting, she could not take potassium iodide by mouth Consequently she was given daily 0 5 to 1 gm of sodium iodide intravenously

On the day after the first dose her pulse was 96 and the vomiting had stopped. She improved rapidly, became ambulatory and was discharged from the hospital ten days later. A metabolic rate determined shortly before discharge was plus 1, but by this time she was thoroughly under the influence of iodine. A cholesterol determination was 155 mg. per 100 cc. of plasma. She has been carefully followed since that time in the Thyroid Clinic. Serial basal metabolic rate determinations have ranged between plus 5 and minus 5. She gained considerable weight and feels stronger. Recently, after a course of propylthiouracil, she was given a treatment dose of radioactive iodine. Except for a brief period during which she had digitalis intoxication, she had done well. Since her discharge her heart continues to fibrillate slowly at a rate of 88.

This patient was so ill when she was first admitted that a metabolism test would have been useless. Indeed, the goiter was dismissed as unimportant until the auricular fibrillation failed to respond to the usual doses of cardiac glycosides and the patient became worse. At this point the possibility of thyrotoxicosis was suggested. Her vomiting precluded a determination of radioactive iodine tolerance. There was insufficient time for a protein-bound iodine determination. Reliance was of necessity placed solely on the clinical findings of globe and lid lag, enlargement of the thyroid and uncontrolled fibrillation. The dramatic response to intravenous iodide and the subsequent course justified the initial diagnosis. This patient illustrates that even with the latest diagnostic methods there are times when clinical judgment is paramount and when long experience with the disease pays dividends.

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A THYROID CLINIC

The following is an edited transcription of a regular Wednesday morning meeting of the Thyroid Clinic of the Massachusetts General Hospital. The patients shown were unselected and the comment was unrehearsed.

CASE I

Dr. HARRY STATLAND: The diagnosis in the first case to be presented this morning is quite obvious. Mrs. C., M.G.H. No. 99029, is a 43-year-old female who was apparently entirely well until about three months ago, when her father died. Shortly thereafter she noticed for the first time that she had become very nervous and had a tremor of her hands. She began to lose weight, and has lost about 10 pounds in the intervening time. She has become intolerant of heat, perspires excessively, but has noticed no change in the prominence of her eyes, nor has any of her family commented on this fact. She has, however, had increased tearing of both eyes. The physical examination discloses that she is quite definitely thyrotoxic. There is a marked tremor of her hands and tongue, and the hands are warm. The eyes seem a little prominent. The thyroid is about three times normal size, is diffusely enlarged and the right lobe is larger than the left. Two determinations of the basal metabolic rate have been plus 76 and plus 68. She is presented this morning not as a diagnostic problem but for the clinic to decide what is the best form of therapy for her.

Dr. JOHN STANBURY: Her palms are warm and a little moist, her pulse is rapid and regular. The thyroid is about three times normal size and is firm. Just to the right of the midline and projecting upward from the thyroid is a finger-like pyramidal lobe. There is a little discoloration around the eyes. (To the patient) Has your skin color changed or become darker?

Mrs. C.: Yes, I think so.

Dr. STANBURY: Where were your parents born?

Mrs. C.: In Italy.

Dr. OLIVER COPE: Of what did your father die? Did he die quite suddenly?

Mrs. C.: He died of old age. He was ninety-three and had been ill for a few years.

DR STATLAND For about eight months this patient has had a chronic scaling dermatitis of the palms This has been diagnosed by the Skin Department as a contact dermatitis, possibly due to the strong soaps which she had been using at home It has not improved Do you think these changes could be in any way associated with the thyrotoxicosis?

DR COPE It would be unwise to exclude thyrotoxicosis as a factor influencing the dermatitis We have occasionally seen darkening of the skin in Graves' disease It is described in the older textbooks Dr Cogan, what do you make of the patient's eyes?

DR DAVID COGAN These eyes seem to be quite typical of Graves' disease There is no edema of the lids nor any considerable injection of the conjunctiva It is not the type which we would classify as hyperophthalmopathic Graves' disease Increased tearing is frequently an early complaint in these patients

DR STANBURY Would you anticipate any trouble following thyroidectomy?

DR COGAN I don't think so I don't think we have seen any patient who has had the ordinary eye signs of Graves' disease go over into the hyperophthalmopathic type following thyroidectomy I think the two entities are distinct and can be separated early *

DR COPE I should like to comment about the disproportion of the enlargement of the thyroid in this case Her goiter has a classic normal distribution The right lobe is larger than the left This is generally true of the normal gland as well as of the hyperplastic gland when the hyperplasia is symmetrical I emphasize it because the disproportion is sometimes taken to mean a neoplastic process in the right lobe At times one sees the disproportionate enlargement of the two lobes to a much greater degree than is evident here This patient presents a classic hyperplastic Graves' gland

DR STANBURY What form of therapy are we to employ here? We have three choices We can either carry her along on propylthiouracil for an indefinite period of time, or we can treat her with radioactive iodine, or we can prepare her properly with propylthiouracil and iodine and then have a subtotal thyroidectomy done May I suggest that we should like to add her to a series of patients on whom we are studying the function of the adrenal cortex in Graves' disease and during therapy with propylthiouracil The plan of study is to make what measurements we can of the function of the adrenal cortex in such patients, to put them on propyl-

* All members of the clinic are not in agreement with Dr Cogan on this point Ed

thiouracil for a period of time until they are euthyroid, and then to repeat these studies in an effort to determine not only the effect of the disease on the adrenal cortex, but also of the effect of propylthiouracil on the adrenal cortex. Some years ago Marine pointed out that these drugs have a peculiar suppressing action on the adrenal cortex, and recently others have shown that the function of the adrenal cortex is diminished after the administration of propylthiouracil. We would anticipate that at the conclusion of such a study the patient would be euthyroid, and would be ready either for continued drug therapy, for radioactive iodine therapy, or for subtotal thyroidectomy. In this particular patient, because of her age, I would be inclined to think that the treatment of choice would be subtotal thyroidectomy. If the clinic agrees, we will proceed with this plan of management.

CASE II

Dr. Lahey Clinic. The second patient is Mrs. P., M.G.H. No. 661819. She is very similar to the patient we have just seen. She is a 23-year-old housewife and a British war bride. Her symptoms date back five months to January of this year, when she became nervous, irritable, and developed a tremor of her fingers. She had lost a little weight in the previous few months, and had been seen by her family physician who told her she had a goiter. He made two determinations of the basal metabolic rate and found them to range in the neighborhood of plus 30.

The patient has a very interesting background. During the war he was with the British Army in a radar detection unit in an area which was subjected to frequent bombings. In 1945 she married an American soldier and the following year she came to this country. She has not been happy. She does not get along at all well with her in-laws, who chide her frequently because of her inability to cook and so on, the way her sisters-in-law do. Recently she and her husband moved to a house which they cannot afford and this has been attended by considerable financial worry. She has a stare and a definite tremor. Her skin is warm and moist. Her pulse is about 120. Her thyroid is enlarged a minimum to that of the previous patient. It is a little larger on the right side.

Dr. Lahey. She has decreased thinking, doesn't she? Again here I think there is no evidence of hyperphthalmic type of Graves' disease. The eyelids show the eyes are not excessive and there is only some dilatation of the veins at the lateral canthi. In all these patients have full range of motion, whereas the larger

ophthalmopathic eye moves with difficulty I do not think that ophthalmoplegia occurs in classic Graves' disease, but it is one of the cardinal findings in the hyperophthalmopathic type of Graves' disease This patient clearly has the classic type

DR COPE The disproportion between the two lobes of the thyroid is not as obvious in this patient as it was in the last, but nonetheless it is present If this patient is to be studied intensively in the hospital, as was decided for the previous patient, I should like to suggest that we have one of our psychiatrists make an intensive study of her while she is here We have repeatedly seen severe psychic trauma as the precipitating or the apparently precipitating event in Graves' disease Both of these patients have had problems immediately preceeding the beginning of their symptoms Perhaps it takes the peculiar combination of a particular kind of psychic trauma in an individual constitutionally predisposed to the disease in order for thyrotoxicosis to follow an emotional upheaval We simply do not know and here may be an opportunity to find out a little more

DR STATLAND Since the last war there have been several reports of the low incidence of thyrotoxicosis in the American and British Armies There was also a low incidence in Holland which suffered heavily during the war And yet in Norway and Denmark, which were comparatively little affected by the fighting, there were epidemics of thyrotoxicosis One wonders therefore about the relation of psychic trauma to the onset of Graves' disease Recently, Meulengracht raised the question again of whether there may be an infectious etiology in these epidemic cases and cites some evidence in favor of this theory

DR COPE Of course this has been argued I think the suggestion that it is an infectious disease is very interesting but it doesn't appeal, because one finds the disease in one type of individual and in one type of situation One may find it as a hereditary manifestation, but one rarely finds it endemic within a family or group of neighbors

DR STANBURY The only well-documented historical epidemic of Graves' disease is the Denmark epidemic which has been reported by Meulengracht and his associates While it is certainly possible that this may have been an epidemic of an infectious agent, it is also possible that dietary factors peculiar to the local situation may have been responsible Certainly this disease does not follow the usual course of an infectious disease The laboratory findings are not in accord with an infectious disease, either The

lymphocytes are usually a little increased in the peripheral blood, and curiously there is frequently a lymphoid hyperplasia through the body. Dr. Stall here has done a few absolute eosinophil counts on patients with thyrotoxicosis and during therapy with propylthiouracil. He has found that the eosinophil count is usually low initially and gradually rises as the patient improves. From this one would expect diminished quantity of lymphatic tissue and diminished lymphocytes in the peripheral blood, and it is paradoxical that it is not so, but perhaps it is explicable as a secondary manifestation of chronic, alarming stimuli.

Dr. Cori: I'm thought that this might be an infectious disease is very interesting. One would then have the disease initiated in the thyroid. Of course this disease goes on for years, and if we do not treat it we know what is going to happen to the patient. He may burn himself out after four or five years. It isn't like any virus diseases we know of. One might think that it would be similar to the virus of infectious hepatitis, but this leads to necrosis in the liver whereas there is no necrosis in the thyroid of Graves' disease nor is there hypertrophy of liver tissue, whereas there is hypertrophy and hyperplasia of tissue in Graves' disease.

Viruses may cause disease of the pulmonary tree, and there may be increased activity of the epithelial cells for a time, but nothing ever comparable to what happens in the thyroid. One doesn't get a hypertrophy of the lungs for instance.

I don't like the idea because thyrotoxicosis doesn't follow the natural history of any of the virus diseases that we know, unless one wishes to think of cancer as an infectious disease. If you are going to call the milk factor in breast cancer an infectious disease then I will have to take it all back.

Dr. Stadnicky: To get back to the patient, may I suggest that we include her as we did the first patient in our study of adrenal cortical function in thyrotoxicosis.

CASE III

Dr. Marvin: The third patient this morning is Mrs. [illegible], M.G.H. No. [illegible]. She is a 55-year-old housewife who comes to the hospital because of a mass in her neck. Eight months ago, after an episode of minor psychic trauma, she began to experience nervousness and palpitations. However, she has had no heat intolerance or loss in weight, and no change in bowel habit. Recently her attention was called to the fact that she had a mass in the neck and she felt a tense feeling in the throat. On examination, the

her palms are warm and moist She has no eye signs suggestive of Graves' disease Her thyroid is enlarged A basal metabolic rate done several days ago was plus 30, and today without any therapy intervening it is plus 16 She has gained 3 pounds in the interim She is being presented today for opinion regarding the nature of the mass in her neck and the appropriate therapy for this condition

Dr Hamlin This is a low lying gland which seems to me to be entirely normal on the left side The right lobe is enlarged about two to three times normal and is quite firm, elastic and nontender It moves well with swallowing I should believe it to be a separate nodule I can feel no pyramidal lobe nor are there any glands palpable in the neck I should say this nodule is about 5 by 6 cm in size

Dr Cope It is frequently true that one can tell a great deal about the nature of the growth in the thyroid simply by observing it as the patient swallows

Dr Lerman The patient doesn't impress me as being thyrotoxic Her face is calm

Dr Cope The problem in this case is whether this is a neoplastic lesion or a nodular degeneration of a previous process Does this patient have thyrotoxicosis? I am not sure, but I think so We ought to be able to tell not only by observing the patient's general appearance, but also by feeling the thyroid, because if this nodule is hyperactive and secreting an excess of thyroid hormone, then the left lobe and the isthmus should be atrophic Our failure to identify clearly the isthmus and the left lobe suggests that the patient has an active nodule I think the physical findings do indicate that the lump on the right side is actively secreting thyroid hormone Radioactive iodine study is ideal to clarify this The patients can be given a dose of radioactive iodine which will tend to localize in the tissue of the thyroid which is actively secreting hormone If this nodule on the right side is overactive, we should be able to ascertain this fact by counting the various areas in her neck with a Geiger counter I presume that she is going to have a tracer dose of radioactive iodine and that various areas in her gland will be counted with the directional counter

Dr Stanbury Assuming that this is a "hot nodule," one might anticipate that this patient would respond very slowly either to iodine or to propylthiouracil What theory would you propose to account for this observation, Dr Cope?

Dr. Cope: All thiouracil does is to hold up the new formation of hormone. If there is a lot stored elsewhere in the gland then the rate of output of the hormone may not be affected by thiouracil in any way whatsoever for a long period of time and I am not sure that the leak of hormone from involuted acini is influenced appreciably by iodine.

Dr. Stanbury: We have been talking about this problem recently and are a little confused. I think it possible that iodine might prevent the leak of hormone from involuted acini. If this is so one might anticipate a better response if thiouracil and iodine were used together rather than separately. I don't know that we have tried the combination in any of our patients here within recent times.

Dr. Lahey: I had a patient recently with just this problem and I treated her with iodine and thiouracil and got into trouble. Her basal metabolic rate did not change and some enlargement of the thyroid occurred, with tracheal compression.

Dr. Cope: In this part of the country toxic adenomas of the thyroid are quite rare, and we have repeatedly made this diagnosis only to find that we have been wrong. We are doing much better now that we have radioactive iodine as a tool for the physiologic investigation of these nodules.

CASE IV

Dr. Malloy: Mrs. D., M.G.H. No. 519241, is a 41-year-old housewife with recurrent thyrotoxicosis who is now in the eighth month of pregnancy. She first developed thyroid disease in Philadelphia about eight years ago. She had a thyroidectomy and her symptoms were relieved. Five years ago, shortly after she was divorced and remarried, she became pregnant and noticed a return of symptoms. She was intolerant of the heat, was nervous and had palpitation. These symptoms smouldered along until about a year ago, when she complained of severe frontal headaches, weight loss and an increased intolerance to the heat. A metabolic rate at that time was plus 17. She was given methylthiouracil for a month and her metabolic rate dropped to minus 6. She had a second thyroidectomy. Unfortunately, a small amount of tissue was removed at this time and her symptoms were not relieved.

During the operation the patient's metabolic rate rose slowly to plus 16. She was given potassium iodide and the rate slowly dropped until the fall of 1948, when she again became pregnant. The rate still stood at plus 5 at that time. Her symptoms were

practically disappeared, but now in the eighth month of her pregnancy the rate is plus 18 At the present time she has a small amount of firm thyroid tissue on the right side and this seems to be a little larger than it was nine months ago Her pulse is 94 and she has a slight tremor Her face is flushed, but it has always been so In general she feels quite well She is being presented to the clinic at this time for evaluation of her case and for opinion as to whether the increase in basal metabolic rate is a physiological response to her pregnancy or whether it represents a return of thyrotoxicosis and as such demands treatment

Dr Lerman Her face is indeed flushed and her pulse is a little fast but her palms are not those of a patient with thyrotoxicosis and she has no eye signs

Dr Stanbury How much of an elevation in the basal metabolic rate would one expect in a normal pregnancy?

Dr Selwyn Taylor Would not the fetal tissue with its high rate of metabolism account for a considerable part of the elevations noticed during pregnancy? What does the protein-bound iodine content of the blood do during pregnancy?

Dr Stanbury Dr Riggs has determined this in a few pregnant patients and I think finds that there is an appreciable though not striking rise in the protein-bound iodine content of the blood during this period

Dr Lerman The basal metabolic rate goes up 25 to 28 per cent in a normal individual during pregnancy The amount of increase that the fetus contributes is very little and probably does not account for more than a 5 per cent increase The rise shown by this patient is entirely consistent with her pregnancy If patients do not have a rise in metabolic rates early in pregnancy the obstetricians consider this a danger signal and find that spontaneous abortion is very common in such patients I think the group at Yale has shown this recently For such patients the addition of thyroid extract early in pregnancy is quite necessary

Dr Stanbury I wish we knew more about the curious relationships between thyroid and pregnancy Certainly the metabolic rate goes up and the hormonal iodine in the blood goes up, and if it doesn't the patients get into trouble Also the thyroid enlarges slightly during pregnancy, and it is a common story from women with single nodules of the thyroid that these nodules first became apparent during pregnancy We need to devote more study to these relationships

PROBLEMS IN THE DIAGNOSIS AND MANAGEMENT OF MYXEDEMA

JACOB LERMAN, M.D.

The diagnosis of myxedema, once attention is called to it, is relatively easy. Often it can be made simply on inspection. In a few instances, the diagnosis is difficult because the disease simulates other entities, or is complicated by another condition. Moreover, as has been emphasized in this Clinic in recent years,[1] and by others,[2] it is no longer sufficient to make a diagnosis of myxedema without qualifying it further as to origin. Before treatment can be undertaken, it is imperative to answer the question, Is the myxedema due primarily to destruction of the thyroid, or is it due secondarily to destruction of the pituitary? Thyroid hormone cures the first but may do harm to the second. Consequently, when a diagnosis of myxedema is made, it is necessary to establish its origin by history, physical examination and various laboratory procedures.

The two patients to be presented will illustrate some of the problems involved.

CASE I. The first patient, F. S., a 54 year old Italian housewife, entered the hospital on January 8, 1949. She was first seen in the out patient department in 1947 because of irregular periods, symptoms suggestive of the menopause, and chronic endocervicitis. She did not return until December, 1948, when she complained of bleeding gums. Presumably the cause was severe periodontal infection. Apparently the bleeding was not due to any hemorrhagic disease. Bleeding and clotting times were normal, platelets were normal, prothrombin time and Rumpel-Leede test were normal. Bleeding from the gums was finally controlled by the dentist by means of local treatment. While she was being studied in the Dental Clinic one examiner suspected the presence of myxedema.

On admission the patient complained of slowness and sleepiness. Her disabilities had developed so gradually that it is difficult to date them exactly. Two years ago, from [illegible] she had not seen her [illegible] about a year [illegible] of puffiness of her face [illegible] the year before [illegible] extremely sensitive to cold, severely constipated [illegible]

From the [illegible] the Massachusetts General Hospital, Boston.

She also complained of weakness and easy fatigability Her voice has become hoarse in the past two months, and she has been unable to concentrate She has experienced parasthesia of the hands and feet and her doctor has been giving her pills for anemia Her appetite has been poor and in the past four years she has lost thirty pounds in weight

The patient had six uneventful pregnancies and deliveries, none of which was complicated by postpartum hemorrhage One miscarriage at three months occurred twenty-three years ago About two years after the appearance of menopause symptoms, already mentioned, the hot flushes became less frequent and troublesome

Her past history, family history and social history are unrelated to her present trouble

Examination showed a moderately obese woman, with typical myxedematous facies She stayed awake with the greatest of difficulty Her skin was thick, coarse and scaly, her hair was thin and brittle, and axillary and pubic hair was practically absent The tongue was large, voice hoarse, and speech was slow and deliberate The thyroid was not palpable, the heart normal in size, sounds were slow and regular, and there was a harsh, systolic murmur, maximal at the apex Blood pressure was 170/98 The lower extremities showed nonpitting edema

The urine was negative, the blood contained 11 5 gm of hemoglobin per 100 cc , the white blood count was 9600, and the smear was normal The basal metabolic rate was minus 39

A diagnosis of myxedema was made One of our associates wrote as follows "The appearance is that of full-blown, classic, primary myxedema, or Gull's disease Indeed, she looks so cretinoid that one often wonders whether by any chance she is actually a true cretin It is desirable that all the laboratory data be accumulated before therapy is begun " This was done with the following results X-rays of the chest showed normal-sized heart with no abnormal cardiac pulsations The electrocardiogram was normal except for small T waves The protein-bound iodine of the blood was 1 2 gamma per 100 cc , the fasting blood sugar 94 mg per 100 cc , cholesterol 226 mg per 100 cc , sodium 129 2 mEq /L and chlorides 93 mEq /L The last two tests, which are in the range of adrenal hypofunction, plus the absence of pubic and axillary hair, made it necessary to do additional tests to rule in or out the possibility of pituitary myxedema

The excretion of the 17-ketosteroids in the urine was 0 4 mg in twenty-four hours, an unusually low value for primary myxedema The excretion of follicle-stimulating hormone in the urine was less that 6½ mouse units per twenty-four hours, which, at the patient's age, strongly favors a diagnosis of pituitary myxedema The Wilder test was positive for adrenocortical insufficiency, i e , the blood

sodium and chloride went down, the excretion of sodium and chloride in the urine was abnormally high and the patient developed symptoms of adrenal failure. The response of the eosinophils in the blood to the administration of epinephrine also favors this diagnosis. The initial eosinophil count was 210 cells per cubic millimeter. Three hours after the administration of 0.5 cc. of 1:1000 epinephrine subcutaneously, the count dropped to 170 cells per cubic millimeter and four hours after a second dose of epinephrine the count was 193 cells per cubic millimeter. This is considered a negative response. In the presence of a normal pituitary, epinephrine causes release of adrenocorticotropic hormone which, in turn, stimulates the adrenal cortex, resulting in a reduction of the circulating eosinophils to less than 50 per cent of the original value. In the absence of a normal pituitary, such a response fails to take place.

The patient now presents the clinical appearance of ordinary myxedema, yet the weight of laboratory data favors the diagnosis of pituitary myxedema. Treatment must of necessity take this into account and the response to treatment will help in establishing the diagnosis.

This case illustrates the difficulty of differentiating myxedema of thyroid origin from that of pituitary origin. The usual method is to obtain evidence for or against hypofunction of the pituitary. A history of postpartum hemorrhage, or onset of amenorrhea without menopause symptoms, or brain trauma is of help. The presence of signs indicating hypofunction of the gonads or of the adrenal glands is also useful. Finally, and perhaps most important, are the laboratory procedures which measure hypofunction of various tropic hormones of the pituitary or hypofunction of the other endocrine glands. A test for thyroid stimulating hormone, which, unfortunately, is not available at present, would be very useful in the differential diagnosis of these two conditions.

Case II.—The second patient, M. Mels, a 70 year old Russian male, was admitted to the hospital on November 1[illegible] 1948 because of dizziness, fatigue and edema of the legs of one year's duration. Sensed [illegible] gradually and were worse in recent [illegible] weeks before admission. He developed edema [illegible] degree [illegible] and [illegible]

He [illegible] to the fact that [illegible] [illegible] [illegible]

[illegible]

"puffy" folds about the eyes The hands and feet were cold and cyanotic, and the neck veins distended The heart was enlarged, grossly irregular and the heart sounds were rapid and weak The blood pressure was 120/95 The lungs showed moderate congestion at the bases, the liver was enlarged, the extremities showed pitting edema up to the knees and there was stasis dermatitis of feet and ankles The urine showed a very small amount of albumin and a few pus cells, the red count was 3 86 million cells, the white blood count 6000 cells, hemoglobin 10 5 gm per 100 cc and differential count normal

The admission diagnoses were generalized arteriosclerosis with coronary artery disease, auricular fibrillation, acute and chronic cardiac failure, peripheral vascular disease and bilateral deafness Initial treatment with oxygen, 10 mg of morphine subcutaneously and 1 cc of mercuhydrin intramuscularly relieved her dyspnea considerably She was then digitalized, placed on a low sodium diet and given mercuhydrin several times during the first week

Additional data obtained are as follows The electrocardiogram confirmed the presence of auricular fibrillation X-ray of the chest showed fluid in both pleural spaces, bilateral pulmonary congestion, enlarged heart and elongated, tortuous aorta The blood nonprotein nitrogen was 28 mg per 100 cc , sugar 94 mg per 100 cc , chloride 97 mEq /L , total protein 6 5 gm per 100 cc and albumin-globulin ratio 1 8

After five days of this regimen, the patient became drowsy and was aroused with some difficulty Her lungs were clearer, edema diminished and dermatitis of legs cleared She became nauseated in spite of omission of digitalis, vomited, and seemed to have lost contact with her surroundings She ate little and her tongue becaue red and smooth Blood drawn six days after admission (November 23, 1948) showed a nonprotein nitrogen of 18 mg and total protein of 5 gm per 100 cc , sodium of 109 mEq /L and chloride of 77 mEq /L —a chemical state characteristic of adrenocortical failure

To combat her clinical condition and disturbance in blood chemistry, she was given 1500 cc of 5 per cent dextrose in saline, 10 gm of salt in twenty-four hours, and digitalis was resumed Six to eight hours after beginning of this treatment, she felt and looked better The next day, the blood sodium was 117 mEq /L and blood chloride 82 mEq /L The same regimen was continued for several days, and on November 29, 1948 the blood sodium reached 125 3 mEq /L , and the blood chloride 87 mEq /L The blood potassium was normal at 4 7 mEq /L and the blood cholesterol at 212 mg per 100 cc

Studies on the urine during this period revealed that she was excreting an abnormal amount of salt Gradually the blood sodium and chloride became normal, she became more alert and lost all evidence of congestive failure At this point it was discovered that her basal metabolic rate was minus 33

Because of the abnormal behavior of electrolytes, the patient was transferred to the Research Ward for further study. Mention is made in the record of three possible clinical conditions to account for such fluctuations, namely, panhypopituitarism, primary adrenal failure (Addison's disease) and "salt losing" kidney. On December 9, 1948, she was seen in consultation by Dr. Maloof and me. Questioning her further, we found that her diet did not contain an undue amount of goitrogens, and she had not taken any drugs which might have an effect on the thyroid. Her periods had stopped at 46 years of age and she was not sure that she had not finished. She had been intolerant of cold for about two years, her hair had become brittle and was falling out, and her skin had become dry. Examination showed a pale, masklike, wrinkled facies, fine, scanty hair over scalp, no axillary or pubic hair, dry, pale skin without pigmentation, a red smooth tongue, general malnourishment and slow fibrillation. Her basal metabolism was minus 39.

It was our opinion that she had hypopituitarism and that salt restriction, mercurial diuretics and dehydration had thrown her into adrenocortical failure during the initial treatment of her congestive failure.

We suggested further studies to confirm this diagnosis. Subsequently the excretion of 17 ketosteroids in the urine was found to be 0.6 to 1.5 mg. for twenty-four hours and of follicle stimulating hormone less than 6.5 mouse units per twenty-four hours. The response of the circulating eosinophils and of the urine acid and creatinine excretion to the administration of a test dose of adrenocorticotropic hormone (ACTH) was equivocal.

The patient was observed on a high high salt intake (18 gm. of NaCl daily) for about four weeks, allowing edema fluid to accumulate. Throughout this period the electrolytes in the blood were nearly normal—the blood sodium was 145 mEq./L., blood chloride 102 mEq./L. and blood potassium 5.[illegible] mEq./L. On January 6, 1949, salt was omitted. Within the next two weeks edema diminished but the blood sodium dropped to 119 mEq./L., the blood chloride to 80 mEq./L. and she became drowsy—an effect equivalent to that of a prolonged Wilder test. Consequently, salt was resumed and again she improved. This time, however, the improvement was not maintained and 11 days a month after the period of salt restriction, she is still drowsy but not as tense, uncommunicative and disoriented. Her blood electrolytes are as follows: sodium 102.[illegible] mEq./L., chloride 6[illegible] mEq./L., carbon dioxide 27.8 mEq./L. and non-protein nitrogen 18 mg. per cent.

[illegible] tells us that [illegible] proof of adrenocortical failure is a characteristic of primary hypopituitarism. Quantitative [illegible] failure [illegible] cycle as [illegible] happens

in this type of case—what is good for her adrenals is bad for her congestive failure Moreover, it is possible that prolonged depletion of salt may result in a state of adrenocortical failure which is irreversible

In the treatment of this patient, one must steer between the danger of adrenocortical failure on the one hand, and of cardiac failure on the other A normal intake of sodium chloride (10 to 12 gm) should be maintained Desoxycorticosterone acetate, 5 to 10 mg daily, should be given for a few days, followed by adrenocortical extract, 10 to 20 cc intramuscularly daily for several days, until the patient is improved Later this may be replaced by testosterone propionate, 25 mg twice a week intramuscularly, or by adrenocorticotropic hormone if it becomes available At the same time she should receive thyroid hormone, 15 mg daily for a week to ten days and increased to 30 mg thereafter An adequate intake of food should be maintained

CONCLUSIONS

These two cases illustrate several important points in the management of myxedema It is important to realize that it is difficult to differentiate between myxedema due to thyroid failure and myxedema due to pituitary failure Before therapy is undertaken it is necessary to resort to all available diagnostic procedures in order to establish the origin of myxedema Moreover, pituitary myxedema is easily overlooked, especially when complicated by another condition When complicated by congestive failure, the management of pituitary myxedema becomes extremely difficult Any measures used to control congestive failure may precipitate adrenocortical failure Finally, a prolonged state of adrenocortical failure in hypopituitarism is probably dangerous because it may become irreversible in spite of vigorous therapy

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THE MANAGEMENT OF AURICULAR FLUTTER

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Auricular flutter is an important cardiac arrhythmia. It is usually associated with organic heart disease, and it is often difficult to correct or to control. In this report are summarized the diagnostic signs useful in its recognition, together with a discussion of the current practice at this hospital in the use of digitalis preparations, especially digoxin, in the treatment thereof. Two cases of auricular flutter, one with and one without congestive failure, will serve as a background for discussion.

PROTOCOLS

CASE I.—*History.* S. I. (MGH No. 28780), a 52 year old housewife, entered the Massachusetts General Hospital for the *fourth* time because of shortness of breath and rapid heart *action for four* days prior to entry. At the age of 15 the patient had a febrile illness which appears, *in retrospect*, to have been rheumatic fever. At the *age of 34* she had been observed at this hospital to have the murmurs of mitral stenosis and regurgitation and aortic regurgitation. Five years before entry she first developed symptoms of congestive failure and was placed on digitalis, a low salt diet, and ammonium chloride, with some improvement. Thereafter she was never fully free from mild symptoms of chronic congestive failure, in part owing to her inability to adhere to instructions. One year prior to her most recent entry she spent two weeks in the hospital because of severe congestive failure. During the intervening year the patient led a very restricted home existence with one short Emergency Ward admission for diuresis. Three weeks before entry she caught cold [illegible] followed by a gradual increase in her symptoms of congestive failure, and four days before entry she developed paroxysmal nocturnal dyspnea. She entered the Emergency Ward again and was found to be in severe congestive failure.

[illegible] temperature [illegible] pulse 150, respirations [illegible] The patient was a pale, chronically ill woman, propped upright in bed [illegible] There was marked [illegible] Her neck veins were distended to the angle of the [illegible]

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*From the Department [illegible] Massachusetts General Hospital [illegible]

mandible, with four venous pulsations visible in each cycle, together with a deep systolic jugular pulse The lungs showed numerous fine and medium moist rales over both lower lobes and signs of a small amount of fluid at both bases, right greater than left The heart was markedly enlarged to the left and right, with the point of maximal impulse in the midaxilla in the sixth left interspace The rate was 150 beats per minute and perfectly regular, in contrast to the previously recorded auricular fibrillation Signs of mitral stenosis and regurgitation and slight aortic regurgitation were present The abdomen was soft without evidence of fluid, the liver edge was felt 4 cm below the right costal margin There was 2 plus pitting edema of both ankles

Laboratory Findings The urine was normal except for specific gravity no greater than 1 015 Hemoglobin 14 gm per 100 cc White blood cells 10,850, with 64 per cent polymorphonuclears and 33 per cent lymphocytes Blood sodium, 129 5 mEq/L , chlorides, 93 mEq /L , nonprotein nitrogen 39 mg per 100 cc , prothrombin time, 18 seconds, with a normal of 15 seconds, or 70 per cent of normal X-ray of the heart demonstrated a greatly enlarged left ventricle and left atrium, with accentuation of vascular markings in both lung fields and fluid present in both costophrenic sinuses An electrocardiogram showed auricular flutter with a ventricular rate of 150

The patient was admitted to the hospital for treatment, which will be detailed in her hospital chart later in this discussion

CASE II —*History* G C (MGH No 638365), a 52 year old housewife, entered the hospital for study because of tachycardia, with a presumptive diagnosis of thyrotoxicosis Four years before entry she had been treated in a local hospital for "acute inflammation of the heart," characterized by cough, shortness of breath, edema of the abdomen and lower extremities, and generalized weakness She had improved on digitalis but remained abed at home for three months and required a full year for convalescence, during which time she had been much limited by episodes of weakness, dizziness, palpitation and rapid heart action, coming on especially under emotional stress Early in this period she had omitted digitalis because of nausea and vomiting Three years before entry, after a single basl metabolic rate determination of plus 38, she was started on iodine solut on, 10 drops three times daily While on this treatment she returned to housework and practical nursing, but because of recurrent severe palpitation and a sense of suffocation she had to avoid crowds, movies, trolleys, and strenuous activity of any sort, physical or mental Under these limitations she got along adequately until one month prior to entry when her attacks of tachycardia became greatly prolonged and were accompanied by orthopnea, ankle edema, and vague sub-

sternal discomfort. She was then readmitted to the local hospital, where iodine was omitted and she was redigitalized. After two weeks however, digitalis was again stopped because of nausea and vomiting and she was referred to this hospital for evaluation of her tachycardia, anxiety attacks, and thyroid status.

Physical Examination. Temperature 98.6° F., pulse alternated abruptly between regular rhythms at 150 and 75 beats per minute, respirations 20, blood pressure 140 mm. systolic and 65 mm. diastolic. The patient lay comfortably in bed. She was slightly obese, somewhat apprehensive, but not tremulous, with warm dry skin and no eye signs of thyrotoxicosis. The thyroid gland was not remarkable. The lungs were clear. The heart was at the upper limits of normal by percussion, with forceful precordial pulsation. P_2 was greater than A_2. The rate dropped abruptly from 150 to 100 on carotid sinus massage, with rapid return to 150 when pressure was removed. There was a Grade I high pitched, somewhat harsh, apical systolic murmur, well transmitted to the left axilla. There was barely detectable ankle edema.

Laboratory Findings. The urine was normal. Hemoglobin 15.4 gm. per 100 cc. White blood cells 7,600, with 59 per cent polymorphonuclears, 29 per cent lymphocytes and 10 per cent monocytes. Fasting blood sugar 85 mg. per 100 cc., total proteins 6.9 gm. per 100 cc., cholesterol 238 mg. per 100 cc. Two basal metabolic rate determinations were minus 6 and minus 17. X-ray and fluoroscopy of the heart demonstrated slight left ventricular and left atrial enlargement, without evidence of pulmonary congestion. An electrocardiogram showed auricular flutter with 2:1 block and a ventricular rate of 150.

ETIOLOGY

Auricular flutter may be seen in an otherwise normal heart, but in most cases organic heart disease is present. The two commonest grish-pening affections are rheumatic heart disease and coronary heart disease. Less frequently thyrotoxic or syphilitic heart disease is present. Occasionally an acute infection, such as pneumonia, underlies the arrhythmia; under these circumstances flutter is usually ephemeral, spontaneously reversible, resistant to treatment, and generally does not recur.

MECHANISM

[illegible]

wave, this wave is unidirectional, it pursues its own wake and passes back to and over the same path again and again "[1] Recent studies of Prinzmetal using high-speed photographic methods suggest that a different mechanism may underlie auricular flutter and fibrillation The details of this work have not yet been published

DIAGNOSIS OF AURICULAR FLUTTER

Suggestive Evidence From History —1 A history of sudden onset, and perhaps of more than one attack with sudden onset and termination, is suggestive of a cardiac arrhythmia, although not, of course, limited to auricular flutter

2 Recurrent episodes of palpitation, and rarely even fainting, can be the result of cardiac arrhythmia, although again not restricted to auricular flutter

3 Long persistence—e g , weeks or months—of a rapid regular heart rate is strongly suggestive of auricular flutter specifically

4 A rapid regular rhythm which suddenly develops in a patient previously observed to have auricular fibrillation will almost always prove to be auricular flutter

Physical Diagnosis —1 *The Pulse* —(*a*) Auricular flutter may be strongly suspected whenever a regular, unvarying, persistent pulse rate in the neighborhood of 150 beats per minute is found

(*b*) Abrupt drop in rate to one half the previous rate, suggesting a shift from a 2 1 to 4 1 block, affords a clue when observed Occasionally one or both of these features may be observed directly from the nurse's chart and a diagnosis made even before seeing the patient

2 *Carotid Sinus Pressure* —Firm pressure or massage on a carotid sinus (the potential dangers of this manoeuver should always be kept in mind) will often produce one of two characteristic results in a case of auricular flutter

(*a*) A sudden slowing to a regular rate at one half or less (depending on the degree of block established) of that present before pressure on the carotid sinus, or

(*b*) A sudden slowing with appearance of marked irregularity of rhythm

Both of these phenomena characteristically tend to revert to the initial rapid regular rate, usually first showing multiple irregular beats before reestablishing the original regular rhythm This reversion helps to rule out paroxysmal auricular tachycardia, which may be abolished by carotid sinus pressure with the appearance of

a slow rate with regular rhythm but which does not revert to a rapid rate when pressure is ended

(c) Deep breathing may have a slowing effect on auricular flutter similar to that of carotid sinus massage

3 *Exercise*—(a) On exercise a slow regular (e g, 4 1 block) auricular flutter may suddenly exactly double to a rate of about 150

(b) A slow irregular flutter (shifting block) which can be confused with multiple extrasystoles or with auricular fibrillation may suddenly become a rapid regular rhythm at a rate of about 150 Auricular fibrillation, on the other hand, tends to become even more irregular with exercise

(c) Slow regular flutter may increase suddenly in rate but be irregular, owing to shifting block In all three instances there is a tendency to prompt and abrupt reversion to the original slow rate when exercise is stopped

4 *Neck Veins*—On inspection it is possible to detect regular rapid flutter waves in the venous pulse in the neck When seen these waves demonstrate an auricular activity two to four or more times faster than the ventricular response observed at the wrist or apex

5 *Variation of the First Heart Sound*—Harvey and Levine[1] have emphasized that with minor changes in the P-R interval, such as are frequently though by no means always seen with auricular flutter the first heart sound on auscultation may be noted to vary considerably in intensity Dock[2] has advanced the hypothesis that this phenomenon is related to the degree of separation of the leaflets of the atrioventricular valves produced by the preceding auricular systole If the auricle contracts too long before ventricular systole (long P R interval) the valves have sagged back to a neutral position if the auricle contracts shortly before ventricular systole (short P R interval), they are not yet fully separated in the ventricle In either instance the closure with ventricular systole does not produce so loud a sound as when the valves are at full separation in the ventricle and have consequently the greatest momentum at the time of closure

6 *Digitalis*—Digitalis and related compounds usually slow the rate of ventricular response in auricular flutter and frequently make the ventricular rhythm irregular (variable shifting block)

Electrocardiogram 1 *Flutter*—The typical feature of auricular flutter is a series of waves of saw tooth configuration The base line at a rate of 240 per minute or half that or twice that exactly the second from the next The shape of the flutter

waves may vary from one patient to another, probably due to different paths of the circus movement in each individual

2 *Carotid Sinus Pressure*—Pressure on the carotid sinus abruptly slows the ventricular response by some definite regular or irregular mathematical factor Pressure does not, however, affect the flutter waves other than slightly, and then only for a second or two of the period of pressure

3 *Pressure of Block*—The usual degree of block in untreated cases is 2 1, but 3 1, 4 1, and higher or irregular types of block are also seen, depending on the functional integrity of the conduction pathway

4 *Precordial and Esophageal Leads*—In most instances the F waves are clearly seen in standard leads 2 and 3 Occasionally, however, they may fail to show a characteristic pattern in the usual leads, and it has been found useful in such instances to obtain a unipolar precordial "special auricular" lead, with the exploring electrode in the third right interspace at the right sternal border Rarely an esophageal lead may show F waves clearly when other leads fail

TREATMENT OF AURICULAR FLUTTER

Although at times quinidine may prove effective in abolishing auricular flutter, general experience has been that more often than not these patients are resistant to quinidine Digitalis and its purified derivatives have proved more reliable, especially in very sick patients where therapeutic dosages are better tolerated and more rapidly effective For this reason we give digitalis first in an attempt to produce auricular fibrillation or to slow the ventricular rate by increasing the degree of auriculoventricular block Following this, an effort may or may not be made to convert auricular fibrillation to normal rhythm Charts of the hospital courses of the two patients already described, one with and one without congestive failure, will serve as illustration (Tables 1 and 2)

As indicated previously, auricular flutter is considered at this hospital an indication for full digitalization, frequently, if necessary, to the point of mild digitalis intoxication, especially nausea and vomiting Thus, in Case II, there was a history on admission of at least two previous episodes of digitalis intoxication as evidenced by marked nausea and vomiting, the second instance having occurred only two weeks prior to admission and presumably during the same episode of auricular flutter for which she was admitted to this hospital Nevertheless, a full course of digitalis was initiated, employing first digitoxin, for prompt standard

digitalization, then shifting for further increase in dosage to digoxin, which with its more rapid dissipation, provides greater safety to the patient. Again, in Case I, when auricular flutter seemed to be increasing an already severe and chronic congestive heart failure, it was considered imperative to administer additional cardiac glycoside in an attempt to control the ventricular rate. This was done despite the presence of marked anorexia, nausea and vomiting, and despite the patient's already being carried on usually adequate maintenance rations of digitoxin. As before, digoxin was preferred to digitoxin or digitalis for this purpose because of its greater margin of safety.

Mode of Action of Cardiac Glycosides in Auricular Flutter.—Cardiac glycosides are useful in the treatment of auricular flutter because of two specific properties:

1. Slowing of conduction in the auriculoventricular bundle. Consequently fewer impulses pass down the bundle to discharge the ventricles in a given length of time, hence the ventricular rate is slowed.

2. Shortening of the refractory period of the auricular muscle, permitting increase in speed of the circus movement responsible for the flutter and ultimately favoring conversion to the more rapid arrhythmia, auricular fibrillation. Since this latter arrhythmia usually can be slowed to an efficient, although still irregular, ventricular response in the presence of digitalis preparations, an over-all improvement in cardiac function is thereby effected, despite the continued presence of an arrhythmia. Occasionally, as in Case II, a digitalis induced conversion from flutter to fibrillation may spontaneously revert to normal rhythm. Whether a positive effort, using quinidine, should be made to favor such a reversion to normal rhythm will depend on individual circumstances beyond the scope of this discussion.

Digoxin.—Digoxin is a purified derivative of lanatoside C, one of the three cardiac glycosides present in the leaves of the yellow or Digitalis lanata plant, but absent from those of Digitalis purpurea. It is of interest that digitoxin is a purified substance of very similar nature but one which can be derived from the leaves of either type of Digitalis.

Advantages of Digoxin.—1. [illegible]

(a) [illegible]

TABLE 1

HOSPITAL COURSE OF THE PATIENT IN CASE I

Date	Digitoxin (mg)	Digoxin (mg)	Failure	Nausea and Vomiting	Electrocardiographic Findings	Notes
Feb 4	Cedilanid 0 4 IV		+++½			
5	0 2 PO	0 25 PO 0 25	+++	0	Flutter-fibrillation, ventricular rate 150	Flutter waves shown in special auricular lead
6		0 25 0 25	+++	+	Auricular flutter, 2 1 block, ventricular rate 150	
7		0 25 0 50	+++	+++	Auricular flutter, 2 1 block, ventricular rate 160	Cardiac consultant favors continuing digoxin despite nausea since patient is beginning to show 3 1 block
8		0 75	++	++	Auricular flutter, 3 1 block, ventricular rate 150	Auricular rate has increased
9		0 50	+	±		
10		0 50			Auricular flutter, 3 1 block, ventricular rate 110	
11		0 50				Cardiac consultant recommended continuation of digoxin in expectation of either increasing the degree of A-V block or converting the flutter to fibrillation
12		0 50	+	0		
13		0 50				

TABLE 1 *Continued*

14	[illegible]	Ventricular flutter 4 1 and 5 1 block ventricular rate 60–75	
15	[illegible]		
16	[illegible]		
17	[illegible]		
18	[illegible]		
19	[illegible]		
20	[illegible]		An episode of probable nodal or ventricular tachycardia during the night
21	[illegible]	Flutter fibrillation ventricular rate 90	
[illegible]	[illegible]		Patient discharged on digoxin 0 3 mg PO daily
22	[illegible]		

TABLE 2

HOSPITAL COURSE OF THE PATIENT IN CASE II

Date	Digitoxin (mg)	Digoxin (mg)	Nausea and Vomiting	Quinidine Sulfate (gm)	Electrocardiographic Findings
Oct 13	0 4				Auricular flutter, 2 1 block
14	0 8				
15	0 2				
16	0 2		+		Auricular flutter, 4 1 block
17	0 2				
18	0 2			0 2	
19	0 1				Auricular flutter with bigeminy
	0 2				
20	0 1				Probably ventricular tachycardia
	0 2				
21	0 1			0 2	Probably ventricular tachycardia but supraventricular tachycardia with right bundle branch block possible COMMENT *Omit digitoxin* and place on small doses of quinidine
22				0 6	
23				0 6	No change
24				0 6	
25				0 6	No change Duration of arrhythmia and configuration of complexes now make auricular flutter 2 1, with right bundle branch block seem the correct interpretation
26				0 6	
27				0 6	
28		0 25		0 6	
		0 25			
		0 25			
29		0 25	+++	0 6	Auricular flutter, 2 1 and 4 1 block
		0 25			
		0 25			
30		0 25	+	0 6	
		0 25			
31		0 25	++	0 6	
		0 25			
Nov 1		0 25		0 2	Auricular fibrillation, ventricular rate of 75 with digitalis effect
		0 25			
2	0 2				
3	0 3				
4	0 2				Auricular fibrillation, ventricular rate of 55 with digitalis effect
5	0 2				
6	0 1				Normal rhythm 80 with digitalis effect Discharged

(*b*) Establishment of definite standard initial dose and subsequent maintenance dose which within reasonable limits will produce the desired clinical effect in the majority of patients.[4]

2 *Lessened Incidence of Nausea and Vomiting*—Another advantage of digoxin is that it appears to lead to reduced frequency of nausea and vomiting at both therapeutic and toxic levels. In large part this is owing to the great reduction of the factor of local gastric irritation when purified glycosides are used.

3 *Speed of Dissipation*—The commanding advantage of digoxin is speed of dissipation. Digoxin effect disappears in a matter of a very few days, whereas digitoxin is effective at least as long as, and perhaps longer than, digitalis leaf itself.[5] This property of digoxin is applicable to the treatment of auricular flutter in several important ways.

(*a*) As a purified glycoside it permits rapid digitalization for early control of the arrhythmia. On the other hand, individual tolerances are diverse and unpredictable, so that rapid digitalization always carries some hazard of toxicity. In such circumstances a rapidly dissipated preparation such as digoxin, permitting the quickest control of toxicity, is of special value.

(*b*) A full digitalis effect is desirable, and indeed usually essential, in order to increase the degree of auriculoventricular block in auricular flutter or to convert the flutter to fibrillation. In such cases excessive toxic effects may result despite careful attempts at control, and hence a rapidly dissipated drug is highly suitable.

(*c*) The problem of digitalization prior to admission in unknown amounts and with attainment of unpredictable levels of glycosidic activity frequently arises in individuals hospitalized because of auricular flutter. These patients, however, are the very ones who most need prompt, safe control of their flutter, and thus digoxin is the drug of choice.

(*d*) In treating auricular flutter due to active disease, such as rheumatic fever or thyrotoxicosis, higher glycosidic levels are required than in flutter from other causes and the chances of toxicity are greater. Digoxin effect disappears [illegible] [illegible] [illegible]

Digoxin Dosage. [illegible]

rarely even more The amount of digoxin required to control auricular flutter must be determined in each instance by therapeutic trial along the lines described in the foregoing case reports If the degree of block is increased but flutter remains, the patient is best maintained indefinitely on digoxin, because of the narrow margin between sufficient dosage to maintain the slow ventricular response and that dosage which produces excessive toxicity If flutter is successfully converted to fibrillation, any digitalis preparation may be used to maintain control of the fibrillation

Caution —At one point the patient in Case II developed an arrhythmia which was subsequently determined to be auricular flutter with right bundle branch block At the outset, however, the electrocardiogram was thought to show ventricular tachycardia In such an instance treatment for the possible ventricular tachycardia—that is, quinidine and not digitalis—is essential, especially since ventricular tachycardia may be the result of digitalis toxicity initially

SUMMARY

1 Two cases of auricular flutter, one with and one without congestive heart failure, have been presented, and the method of management briefly outlined

2 The major clinical features of auricular flutter have been summarized

3 Certain properties of the purified lanatoside or digilanid C derivative, digoxin, have been described These include rapidity and completeness of absorption of the drug upon oral administration and, of paramount importance, rapidity of dissipation on cessation of administration

4 The advantages of these properties in the treatment of auricular flutter are discussed *

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MANAGEMENT OF ESSENTIAL HYPERTENSION

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The present discussion will be limited to essential hypertension to that condition in which there is no recognizable specific cause of the elevated pressure in head, heart, kidney or the endocrine glands. The hypertensive state is a somewhat nebulous concept because we do not know the primary cause or causes. Hypertension means disability and death to the patient. Unhappily, any degree of hypertension may mean the same to the patient's physician, and if so, he will confirm the patient's worst fears.

When a patient is seen for the first time and his blood pressure is taken, if the manometer registers above the accepted level of normal for blood pressure, we say that patient has "hypertension." What, then, do we positively know? In reality the reading of the manometer only tells us that the intra arterial pressure of the patient's brachial arteries is higher than the accepted normal. The blood pressure level does not convey the constitutional susceptibility or resistance of the patient. In following patients over a number of years one notes a marked variation in this susceptibility and resistance. One patient will be seen with a blood pressure of 230/110 without any symptoms and continue at that pressure for many years without objective evidence of serious organic damage. Another patient will be seen with the same pressure or lower and, after a year or two, will develop definite organic damage in the form of a vascular accident in the head or the heart or serious chronic vascular nephritis.

The latter patient represents the unfortunate constitutional susceptibility which we see all too often and which we tend to associate with an elevation of the blood pressure. The cause of the undue susceptibility we do not understand. We fail to recognize significant differences between benign and malignant, and malignant rapidly advancing, essential hypertension, other than differences in tempo. The former patient has simply an elevated blood pressure with little evidence of curable peripheral vascular disease and the latter patient has an elevated blood pressure with evidence of serious vascular [illegible] of the three vital organs, head, heart, kidneys.

[illegible]

We have found it helpful to formulate grades of hypertension and express the state in degrees of recognizable organic change as a cross section of the natural history of this state, and by interval observation and study to describe the rate of progress, either favorable or unfavorable There are four grades which we recognize [1]

Grade I—Minimal change in the fundi, normal heart or slight prominence of the left ventricle by x-ray, no impairment of renal function

Grade II—Widening of light reflexes, caliber changes and arteriovenous compression The heart is usually prominent in the region of the left ventricle, but without functional impairment There may be slightly impaired renal function

Grade III—In addition to the fundi changes in Grade II, there are often hemorrhages and exudates The heart is markedly enlarged, commonly with symptoms and signs of actual or impending congestive failure The urine frequently shows albuminuria and casts Renal function is often impaired though actual failure is not common Cerebral accident sometimes occurs

Grade IV—The cardinal sign is edema of the optic disks Cardiac enlargement and congestive failure are frequently present Renal impairment and failure are common

It should be realized that these clinical signs are not necessarily correlated with the inward pathological state in essential hypertension, they are simply observable signs that have been found useful for grading purposes

TYPES OF TREATMENT

Conventional Medical Treatment—Current forms of therapy for essential hypertension are based on the use of drugs, modification in diet, surgery and psychotherapy The conventional medical treatment includes sedation, rest, diet and psychotherapy The most frequently employed sedative is phenobarbital in doses of 15 mg ($\frac{1}{4}$ grain) four times a day Phenobarbital is one of the longer-acting barbiturates and serves a useful function in preventing mounting tension during the day, thus promoting sleep at night If insomnia is a problem, one of the more rapidly acting barbiturates of shorter duration may be useful, such as sodium seconal in doses of 0 1 gm ($1\frac{1}{2}$ grains) given a half hour before retiring Wakefulness during the night may yield to sodium amytal in the same

dose. When used in this way, barbiturates have an important place in the treatment of essential hypertension by promoting rest, a fundamental principle of treatment.

When obesity and essential hypertension coexist, a reducing diet is obligatory. Such a diet implies the reduction of the total calorie content, and the most effective way to achieve this is by reducing that component whose calorie content per gram is the greatest, namely the fats. For the best results the patient must not only be instructed in the diet, but should be followed at frequent intervals with thoughtful evaluation of the patient's personality. Some patients of large build and hearty appetites become depressed unless they overeat. Dextrorotatory amphetamine (dexedrine) in doses of 2.5 to 5 mg. ($\frac{1}{24}$ to $\frac{1}{12}$ grain), used cautiously, may control the depression, the appetite, and enable these patients to follow the prescribed diet. Use of a program including these components may in many cases classed as Grade I and Grade II result in a sustained drop in blood pressure. An illustrative case will be described later to show the effect of such a program.

Other drugs used in the treatment of hypertension are the nitrates which act as nitrites, causing peripheral vasodilation. The nitrates are in general unsatisfactory owing to the short duration of action. Potassium thiocyanate, a drug still used by some, has a definite hypotensive effect. This drug has two actions, one similar to the iodides and the other similar to the nitrates, the latter presumably responsible for the hypotensive action.[3] Blood levels should be determined frequently and should not exceed 8 to 12 mg. per 100 cc. It is important to realize that this drug is potentially dangerous and may result in serious toxic reactions.[3]

Rice Diet.—The rice diet of Kempner[4] is a popular one currently and has been found effective in some cases. This is a restrictive diet, most adequate by the usual standards, involving the reduction of protein to 20 gm., fats to 5 gm., salt to 200 mg., while the amount of carbohydrate is increased, varying between 350 and 450 gm. The amount of carbohydrate chosen depends on whether it is desirable for the patient to gain or lose weight, the rapidity of weight change desired, and the degree of tolerance of the patient to tolerate carbohydrates. The calorie content of the rice diet varies from [illegible] calories per day depending on the amount of carbohydrate ingested. The average calorie intake per day is [illegible] calories. It is an [illegible] of the rice diet as used at the Mayo Clinic, Grade II [illegible]

KEMPNER RICE DIET

I *Rice*—Each day use one cup of rice, measured before cooking This yields approximately four cups of cooked rice Brown, polished or white rice may be used Boil or steam without salt, milk or fat (Use no butter, margarine, drippings, lard, grease or salad oil)

II *Fruits*—*Fresh* raw or cooked Any fruit with the exception of avocado pears, dates and nuts may be eaten No tomatoes No more than one banana per day

Canned Allowed, if no preservative has been added Inspect labels Read the fine print which may mention artificial flavor or color, sodium benzoate, sulfur dioxide or corn syrup Do not buy any such

Frozen fruits May be used

III *Sugar*—As desired White only Glucose (dextrose) may be used It is less sweet and better tolerated by many people Honey permitted—but no maple sugar, corn syrup or malasses Fruit and sugar jams and jellies—if pure

IV *Fruit Juices*—Any fresh or canned fruit juice may be used if it contains no artificial flavor, color or preservative Tomato juice and vegetable juice are not allowed

V *Fluids*—Limited to 3 to 4 cups of fruit juice per day After the first three or four days, no additional water should be taken

SPECIAL INSTRUCTIONS Eat only the foods outlined on your diet Do not drink any tonics, root beer, sodas, ginger ale, or other carbonated beverages No beer, ale, wine or whiskey No coffee or tea

All patients who are placed on the strict rice diet must be seen frequently by the physician Frequent and careful observation is absolutely necessary to detect signs of sodium depletion, the physical signs of which are weakness, faintness, fatigue, nausea and vomiting Ideally these patients should have frequent blood chemical determinations, including the serum sodium level Practically, this is, for many doctors, impossible A careful clinical follow-up, however, serves as a good protection for the patient If symptoms suggestive of sodium depletion become apparent, the diet should be modified immediately

There is only one way, in our experience, to determine whether a patient is adhering strictly to the rice diet, namely by frequent determination of *urinary chloride excretion* A simple chemical method to determine the chloride excretion in the urine quantitatively is given below

Reagents (1) 20% K_2CrO_4
(2) 1.7% Sol $AgNO_3$
(3) 1% phenolphthalein in 95% alcohol
(4) 10% acetic acid (by vol.)

Take 10 drops of urine to test tube

Add 1 drop of phenolphthalein

If urine is alkaline, add 10% acetic acid drop by drop until pink from phenolphthalein just fades

Add 1 drop K_2CrO_4

With same dropper, cleaned, as used to measure the urine, add 1.7% $AgNO_3$ drop by drop until yellow color from the K_2CrO_4 turns to rust

Calculations (No. of drops $AgNO_3$ used *minus* 1) times 10 equals mEq Cl⁻/liter urine

Note Use dropper at same angle when measuring urine and $AgNO_3$ so as to assure the same size drop for each

The reason 1 is subtracted from the number of drops of $AgNO_3$ used is because the last drop combines with the K_2CrO_4 to give the color change

The urinary chloride excretion of a patient on an average diet varies between 125 and 175 milliequivalents per litre in twenty four hours, whereas that of a patient on the strict rice diet falls to 10 mEq per litre or below. The shaded area in Figure 231 represent these variations. The two curves show the chloride excretions of two different patients, both of whom insistently maintained that they were eating nothing but unsalted rice, fruit and fruit juices.

It is difficult to predict which patients will show a good response to the rice diet but a conscientious trial is suggested for patients who may be classified as Grade II or Grade III in whom general medical treatment has brought about no modification in the condition. A case described below, a patient who was classed Grade III showed an excellent response. Other patients just as faithful to the rice diet, however, have shown little or no change in blood pressure. Usually there is a symptomatic improvement although the blood pressure may show little change. Some patients seem able to tolerate the diet while others do not have the fortitude to adhere to such uninteresting and monotonous fare. Motivation in adhering to the diet is best accomplished if several patients can be started at approximately the same time and group therapy utilized. Care should never be used as a means of persuading patients to adhere to the diet, the damage done by the use of force can never be eradicated at any price due to its subsequently.

The advantages of the rice diet are that it is simple to prepare, cost little, the patient understand and can be well tested out if the patient is cooperative. The disadvantages are that it is a

monotonous diet, a starvation diet by the ordinary standards and may result in lowered resistance to infection

Low Sodium Diet.—The efficacy of the low sodium diet in the treatment of hypertension has been "proved" and "disproved" repeatedly over half a century Interest in the low sodium diet recently has been revived by Grollman [5] This diet has the usual proportions of all constituents in an average diet with the exception of sodium chloride which is reduced to at least 0 5 gm per day and

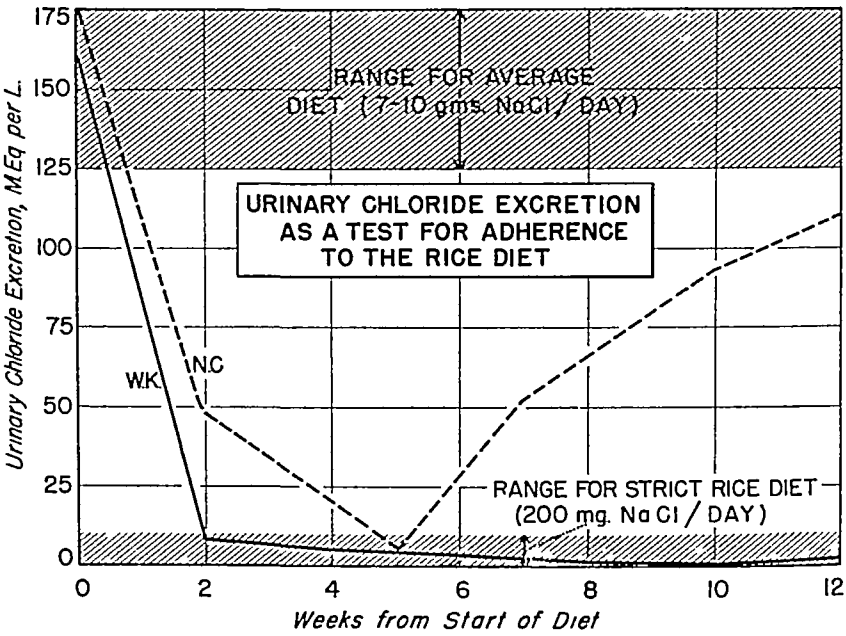

Fig 231 —Urinary chloride excretion on average diet shown by shaded area at the top, on rice diet by shaded area at bottom of figure *W K* and *N C* represent chloride excretions of two separate patients, W K was a strict adherent to the rice diet, N C said he was but actual test showed that he was not

in some instances to 0 2 gm The reduction in sodium chloride is accomplished by preparation of all food without salt, the use of salt-free bread, salt-free butter and salt-free milk (many commercial brands of salt-free milk are available) Patients must be warned against the use of such things as baking soda, baking powder, mustard, catsup, meat sauces, bouillon cubes, margarine, popcorn, pretzels, potato chips, olives, pickles, prepared horseradish, worcestershire sauce, and laxatives such as sal hepatica There are certain vegetables high in natural salt which should be omitted entirely from the diet, and are listed below

SALT CONTENT OF VEGETABLES TO BE AVOIDED

	Mg./100 gm		Mg./100 gm
Beets	110	Celery	110
Beet greens	130	Dandelion greens	76
Kale	110	Sauerkraut	730
Mustard greens	48	Spinach	190

This diet gives much greater variation than the rice diet, hence more patients are able to tolerate it, it has the disadvantage of being more difficult to prepare and is harder for the patient to understand. The same care should be observed in watching patients for any signs of sodium depletion as that exercised for patients on the rice diet. The effectiveness of this diet as a treatment of hypertension has not been clearly established, but the response in some patients justifies a trial after conventional medical treatment has failed, and before the rice diet is used. It should be noted that the rice diet is essentially a low sodium diet with additional restrictions of proteins and fats.

Surgery.—The surgical treatment of hypertension is still widely used, although there has been some decrease in enthusiasm for this treatment in the last few years as more reports appear in the literature.[1, 8] There are several types of sympathectomies, but the most frequently used are the supradiaphragmatic sympathectomy of Peet,[7] and the lumbodorsal sympathectomy of Smithwick.[8] Attempts have been made to develop studies which will predict the response to sympathectomy, but so far these tests have proved to be of limited value. Careful clinical evaluation of each patient is necessary with consideration of age, sex, cerebral, cardiac and renal function. Usually patients under 50 years of age do better. Women generally respond better than men. Patients who have had vascular accidents in the head or the heart, or who have seriously impaired renal function seem to do badly.

Each case needs careful individual evaluation not only as to the hypertensive state, but also consideration should be given to the personality of the patient, and to the social and economic factors involved. Patients in Grade I do well with or without operation, therefore surgery has little to offer. Surgery in those patients in Grade II who have a progressive type of disease sometimes seems to halt the progress of the disease. Patients in Grade III in whom there is clinical evidence of irreversible diffuse arteriolar disease in brain, heart or kidney apparently derive little benefit. The disease progresses in much the same manner as it does in those patients

who have not been subjected to surgery Certain patients with malignant hypertension (Grade IV) without significant cardiac or renal impairment benefit in respect to lowering the blood pressure, increased survival time and symptomatic improvement We feel that the early malignant hypertensive should be urged to accept surgery and without delay

Psychotherapy.—Psychotherapy should form a part of all types of treatment of essential hypertension because, prior to the organic localization, the symptoms are those associated with nervousness or nervous tension and these symptoms are readily relieved by simple measures Many patients come to the doctor greatly distressed because they have been refused insurance or have lost their jobs on the basis of high blood pressure As a rule they are extremely anxious and they fear the worst in the form of a "shock" or a "heart attack" Therapeutic effort should be accompanied by maximum encouragement, emphasizing improvements in the patient's condition and minimizing the possibility of poor prognosis The physician's duty is to allay anxiety and, when successful, this relieves or prevents not high blood pressure, but high blood pressure anxiety Relief of anxiety, in many instances, is happily accompanied by a considerable fall in blood pressure, but as a rule not to normal The most significant thing about the psyche in hypertension is that mental or emotional stresses act as pressor effects but rarely does psychotherapy restore the blood pressure to normal We suspect that mental and emotional stresses belong to the legion of pressor factors which contribute to hypertension in susceptible individuals

ILLUSTRATIVE CASES

The following cases illustrate the use of conventional medical treatment, rice diet, sympathectomy, and psychotherapy

The first case described represents an obese female in the menopause on conventional medical treatment The response both in regard to blood pressure and symptoms was gratifying

CASE I —C P , a 51 year old housewife, was first seen October 21, 1947 with a known duration of increased blood pressure of three years Past history revealed that she had had hypertension associated with severe headache, some impairment of vision, and albuminuria during each of two pregnancies The blood pressure and accompanying symptoms had receded after each pregnancy and she had been well until three years before the first observation Her presenting complaints were fatigue, headache, feeling of pressure in the head, mild

exertional dyspnea and nocturia two to five times. She was overweight. Examination of the fundi showed some tortuosity of the vessels with moderate arteriovenous compression. The blood pressure was 190 mm. of mercury systolic and 130 mm. diastolic. The heart was enlarged to the left, there were many premature beats, and a Grade I basal systolic murmur was heard. The urine analysis was negative, and

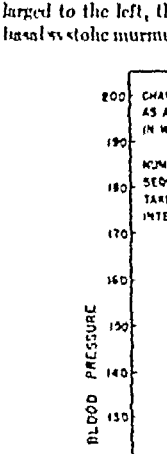

Fig. 231. Change in blood pressure as a function of change in weight in patient [illegible]

the kidney function was normal as determined by the usual kidney function tests.

The treatment consisted of reassurance, reducing diet, [illegible] mg. [illegible] grams [illegible] times a day and [illegible] to the patient was seen at frequent intervals thereafter, about the next fifteen months, during which time she gradually lost 30 pounds [illegible] there was a gradual reduction of blood pressure [illegible] the curve of the blood pressure was [illegible] [illegible] after [illegible] the patient gained [illegible]

defined substances It can of course be argued that if, as SCHRÖDINGER[26] has lately insisted, genes and chromosomes have so much of the physical integrity of molecules that they can be usefully regarded as such, then our individual chromosomes *are* distinct chemical compounds This is the "rather special sense" spoken of above Having acknowledged its somewhat tortuous validity, it can be dismissed

The serological uniqueness of the individual may have some exciting consequences It has for some time been known that in the case of serum-proteins,[27] as well as of red-cell antigens, there is a "one-to-one correspondence between the presence of specific single genes and specific antigens"; and, as a general rule with fairly well-defined exceptions,[28] there is "no evidence for gene interaction, either between allelomorphs or between genes at different loci"[29] Since the serological identification-mark of the individual is such a faithful fingerprint of his gene complex, may one not guess that the antigens themselves are "rather direct gene products"? HALDANE[30] thinks so it is the most economical hypothesis, just as it is the most economical hypothesis to suppose that the voice which comes from the gramophone is made by a little man right inside the box The hypothesis can be put to empirical test, and STURTEVANT[29] has lately shown how For the antibodies produced by these antigen-genes should react with the genes themselves, and either put them out of action or (perhaps less plausibly) cause them to undergo mutation EMERSON[31] has tested this latter possibility with suggestive if hardly conclusive results It is noteworthy in this connexion that the immune system set up by skin homografts very likely acts by blocking nuclear division in the cells of the grafted skin[24] Soon someone will graft skin from one mouse to another which differs from it by only a single gene Will the phenotypic expression of that gene be suppressed in the grafted skin? It is almost a test case In this sort of way, perhaps, serology will give the geneticist the weapon which he most sorely lacks that which the biochemist has in cyanide and iodoacetate, and the serologist himself in the technique of absorption the *specific inhibitor* of gene-determined processes.

26 Schrödinger, E What is Life?, Cambridge, 1944
27 Cumley, R W, Irwin, M R *J Immunol* 1943, 46, 63
28 Irwin, M R *Genetics*, 1939, 24, 709
29 Sturtevant, A H *Proc nat Acad Sci USA*, 1944, 30, 170
30 Haldane, J B S Perspectives in Biochemistry, Cambridge, 1937
31 Emerson, S *Proc nat Acad Sci USA*, 1944, 30, 179

Dr JOHN PARKINSON will deliver the Harveian oration at the Royal College of Physicians of London on St Luke's day, Thursday, Oct 18, at 3 PM He will speak on rheumatic fever and heart disease

Dr P A BUXTON, FRS professor of medical entomology in the University of London at the London School of Hygiene, and Sir ALEXANDER FLEMING, FROP, FRS, professor of bacteriology in the university at St Mary's Hospital have been appointed members of the Medical Research Council

WE have to announce the death of Dr JAMES HENDRY, regius professor of midwifery in the University of Glasgow, on Sept 9, within a few days of his 60th birthday Dr. Hendry was also medical director of the Glasgow Royal Maternity and Women's Hospital, deputy chairman of the Central Midwives Board for Scotland, and a member of the Goodenough Committee.

Annotations

TOO MANY DOCTORS IN THE RAF?

OUR leading article of Sept 8 expressed astonishm at the news that the Royal Air Force proposes to m tain its medical establishment at the same level as du the war—i e, at between 2 2 and 2 3 per 1000 t strength "Civilians," we said, "are no doubt li to exaggerate the difference made by the end of fighting, but this difference can scarcely be negligib We are assured, however, that in fact the med requirements of the RAF remain as great as they w last year or the year before Though during the there were heavy losses in aircrew killed or miss the RAF Medical Service has never had to care for large number of wounded at one particular time th was rather a daily attrition, as the RAF was c tinuously in action In peace the risk of injury du training is as high as in war, since instruction is v intensive, and the proportion of RAF personnel inju at games or in road accidents is much higher Furth more, a larger proportion of the Force is stationed relatively unhealthy areas overseas The general ef of these differences is that the number of admissi to hospital from all causes (sickness, injuries, wounds) has been no greater during the war than in previous years, and cannot be expected to decline w the return of peace At 2 2 per 1000 (1 5 in the Uni Kingdom and Western Europe, including staffs hospitals, boards, teaching and research establishmen and headquarters), the medical establishment of RAF is stated to be lower than that of any other Serv of modern times, in peace or war We are informed th since hostilities ceased a number of hospitals have be reduced in size or closed, and the allotment of medi officers to stations has been lowered, both at home a abroad These economies are offset, however, by n commitments. For example, the quota of patie formerly treated in EMS hospitals will come directly und Service care, men who have developed tuberculo while in the RAF are being treated in the RAF f periods up to 8 months, many medical officers must taken away from their present duties for special trainin (e g, to replace civilian consultants and specialists no being released), and the RAF Medical Service w again have to undertake the care of RAF families on a increasing scale The RAF consists of relatively sma units scattered very widely; it controls huge areas Africa and elsewhere, and on overseas flying routes it ha a great many isolated stations where doctors must kept not only to deal with the unit but also to tre casualties arriving by air, or crashes among the numero aircraft using these staging posts Those bearing th responsibility for efficient medical care at all the points feel that an establishment of 2 2 doctors p 1000 is no more than sufficient for their present need

Clearly the time has come when the various Servic departments should be told what proportion of ou medical resources they may expect to retain or recru To this subject we shall shortly return

PENICILLIN IN RAT-BITE FEVER

LAST October the successful treatment of a case rat-bite fever due to *Streptobacillus moniliformis* w described in our columns by Kane,[1] and in an acco panying annotation[2] the hope was expressed that p cillin therapy would turn out to be equally succes in the spirillar form of the disease This hope ha been realised Wheeler[3] has had the opportunity using penicillin in 5 cases of the disease, 1 of which due to *Spirillum minus* and the rest to the streptobac with gratifying results in all The patients were ha

1 Kane, F F *Lancet*, 1944, ii, 548
2 *Ibid*, p 540
3 Wheeler, W E *Amer J Dis Child* 1945, 69, 215

of ages ranging from 5 weeks to 6 months, and the penicillin was given in 3 hourly injections of 5000 units, continued for 7–10 days—some 300,000 to 400,000 units in all. This is about twice the amount required by Kane for his patient aged 15. It is of interest that all but one of Wheeler's cases were due to the streptobacillus, and other recent American reports of successful treatment of the streptobacillary disease emphasise that this form of the disease is much commoner than the spirillar.

The ages of Wheeler's patients are perhaps surprising to readers in this country, where rat-bite fever is rare and not noticeably commoner in infancy. A paper by Richter[4] from Baltimore analyses a series of 65 patients with rat bites treated at the Johns Hopkins Hospital in four years: all coming from an area of two square miles near the hospital, of whom 7 developed rat bite fever. Of these 65, 60% were babies under a year old, who were bitten while asleep.

Failure to isolate the streptobacillus more commonly has sometimes been attributed to its inability to grow in ordinary media, and the need for special techniques in its isolation. Wheeler claims that isolation is simpler than generally realised: the most important factor is a high concentration of protein in the culture and he uses at least 8 c.cm. of blood to 50 c.cm. of broth.[5] The organism grows as characteristic cotton wool balls. Its ease of isolation is borne out by Kane's experience; he grew it on four successive occasions on Loeffler slopes, and in 50% serum broth.

HOSPITALS AND HEALTH CENTRES

THE *Economist* of Aug. 18 endorses the plea made by the joint committee of the King's Fund and the Voluntary Hospitals Committee[6] for the retention of the small voluntary hospital. Atmosphere, the friendliness of the staff, and a feeling of security are attributes apparently intrinsic in the small unit and alien to the large one, and matter far more "to most patients" than "whether the medical or surgical treatment is the last word in efficiency." This type of argument however is full of fallacies. (If it is not, Heaven help the unfortunate patients who will enter in legions the portals of the 1000 bed teaching hospital, about which the same committee is equally enthusiastic.) The real answer surely is the one given by Gray and Topping in their survey of the hospital services of London. Whatever the terrors of the patient *before* he gets into hospital, once he is admitted his universe is not the 150 or 1000 beds of the hospital but the 20 or 30 beds of his ward, which is much the same in every kind of hospital. And the Really Important People are the sister and staff nurse and the houseman or the resident medical officer, who are much the same whatever the size of the institution.

Our contemporary also applies this argument to health centres: the dingy consulting room of an old family practice," it points out, may be preferred by many a patient to the modern building with secretaries, clerks, card indexes, and other terrifying impedimenta of efficiency. And there is more substance in this application than in the original argument. If health centres are to house six or seven doctors and to have the advantages of clerical assistance and the like, there is real danger that patients may complain of a loss of privacy—indeed of a blaze of publicity. It may even be that for a large group of patients the chief benefit of health-centre practice will be indirect: by the stimulus to professional efficiency which gregarious working conditions will engender in their medical attendant. The fact remains that medical clerks, whether in hospitals or health centres or tuberculosis dispensaries, are not given to betraying confidential information acquired in the course of their work; and once the patient has taken the plunge and got into the centre, the reality will probably prove far more pleasant than the anticipation. To other groups of patients, moreover, the benefits of the health centre will be more immediately apparent. The poorer quarters of every large town contain as the equivalent of the "dingy consulting room" converted shops dignified by the name of surgery. Not much chance of privacy here, even if there is ample scope for verifying the *Economist's* statement that "the most efficient methods are not always the most effective." Ninety per cent. of the population still have an income of less than £400 a year, and among the poorer sections of this substantial portion of the community there should be full opportunity for practical trial of the merits and demerits of all the health centres it will be possible to provide by building or adapting within the next ten years.

To the doctor, the advantages of team work have been increasingly obvious for many years, with the result that private partnerships of two, three, and four doctors have become the rule. The health centre is a vehicle for team work or it is nothing—unless it is a relief to the wife of the doctor who lives in the house with the dingy consulting room of an old family practice.

TOXICITY OF BORIC ACID

IT has long been realised that boron if misused, may cause serious and even fatal intoxication. Since Dopfer[7] first recorded erythema and profound toxemia in a child of 2 treated for a burn by application of 80 grammes of 10% boric acid during four days, a number of similar incidents have been reported. All agree as regards symptoms, which include vomiting, diarrhœa and rapidly progressive prostration, with severe irritation of the central nervous system. Extensive exfoliative dermatitis may develop when the drug is given over a long period, and hæmorrhagic cystitis is not uncommon. Most cases have followed accidental ingestion of substantial quantities of boric acid or borax, but poisoning has been described in infants who have suckled from nipples cleansed with saturated boric acid solution. In some of these cases it has been possible to estimate the amounts given, and it appears that the fatal dose of boric acid in an adult is somewhat more than 15–20 g. and in an infant 5–6 g.[8] It cannot be said that boric acid is very toxic to human beings, for Peyton and Green[9] record recovery after a subcutaneous injection of 28 g., while McIntyre and Burke[10] had a patient recover after 15 g. was given intravenously.

Animal experiments too, indicate that boric acid is not very toxic. Pfeiffer, Hallman and Gersh[11] find that the dosage which kills more than half a group of animals is above 1·2 and less than 3·45 g. per kg. body weight. Dogs tolerated up to 2 g. per kg. orally and rather less than 1 g. per kg. subcutaneously. These, of course, are large doses, and they suggest that animals are more resistant than man to boric acid. Animal observations also assist in the elucidation of clinical features. Signs of acute intoxication include cyanosis, depression, ataxia, fall in body temperature, persistent vomiting and meningism. Short convulsions may precede death. Blood changes in dogs are suggestive of shock with hæmoconcentration, a rising pulse rate, increase in blood non-protein nitrogen and potassium and gradually increased phosphorus excretion in the urine. About 40% of the dose of boric acid is retained in the body for more than 48 hours, and daily excretion of small amounts goes on for some time. The chief pathological changes are renal and nervous; glomeruli and tubules undergo damage and nerve-cells of the cerebral cortex and spinal cord die off. Skin lesions are not uncommon; but the liver is unaffected.

[4] Richter, C. B. *J. Amer. med. Assoc.* 1945, 128, 324.
[5] Wheeler incubated his blood-cultures in a "candle jar." This is a simple device in which a small candle is lit inside a jar with a well fitting lid, whereby a raised CO_2 concentration with lowered oxygen tension, is achieved.
See *Lancet*, Sept. 15, pp. 312 and 315.

[7] Dopfer, *Münch. med. Wschr.* 1905, 52, 763.
[8] McNally, W. D., Rist, C. A. *J. Amer. med. Ass.* 1944, 124, 90.
[9] Peyton, W. A., Green, D. *Stk. med. J.* 1941, 34, 1255.
[10] McIntyre, A. R., Burke, J. C. *J. Pharm. exp. Ther.* 1933, 48, 11.
[11] Pfeiffer, C. C., Hallman, L. F., Gersh, I. *J. Amer. med. Ass.* 1945, 128, 266.

Chronic boric-acid poisoning leads to remarkably little pathological disturbance, although the compound accumulates in the central nervous system—especially the grey matter of the spinal cord and cerebrum—the peripheral nerves, the liver, and the body fat, in that order. The blood-picture remains unaltered and the liver is but slightly affected Growth of young animals is inhibited. Pfeiffer, Hallman, and Gersh show that disturbance of this kind may result from treatment of wounds with an ointment or when serous cavities are irrigated with 5% solutions of boric acid. Under these conditions, most of the compound is absorbed, and a simple calculation shows that in surgical practice quite large amounts of boric acid may be brought into contact with ideal absorbing surfaces

The position, then, seems to be that boric acid has toxic properties, enhanced by its tendency to accumulate in the tissues. A long period (14 to 18 days) is needed for urinary excretion to reach a steady level relatively little is excreted during the first 48 hours, and appreciable amounts persist in the brain and liver for as long as 4 days after stopping the daily dose, indeed boron may accumulate in the brain in amounts greater than in the treated wound On the other hand both human and animal experience show that many grammes must be absorbed before the danger level is reached Hence in attempting to arrive at a guiding principle for the treatment of wounds undue emphasis should not be placed upon results of accidental poisoning So far, clinical evidence of ill effects after wound treatment is scanty; but there does appear to be some need for caution in the use of boric-acid irrigations, as is shown by the case described by Ross and Conway,[12] in which a child of 3, treated for empyema by continuous irrigation with 5% boric-acid solution, developed an extensive rash and signs of profound shock, the organs contained appreciable amounts of boron. As boric acid is only weakly antiseptic, it is worth considering whether a more effective and less potentially harmful agent should be substituted

FOSTER HOMES FOR THE INSANE

THE value of family care for the mentally disordered is universally admitted, yet little attempt has been made in this country to find suitable foster homes for the purpose. In the family care of defectives much more has been achieved In the State of New York the development of foster family care for the insane has been unusually successful because of the energy and forethought exercised in this uphill but rewarding work. Miss Crutcher, the director of social work in the New York department of mental hygiene, has written a book[13] which in its practical and restrained enthusiasm, and in its protocols of success, shows that she is in the tradition of those Victorian women who could make politicians and State agencies serve their idealist purposes She points out that the therapeutic work of a mental hospital is hampered by the deadweight of patients who have no hope of full recovery but nonetheless require continuous care. Family care is a method of returning into the community those who have improved somewhat and are harmless, but whose own families could not take charge of them Besides the advantage to the patient, it is an effective administrative procedure since it releases hospital space for patients who need active treatment and for patients who could not be allowed to live outside; it is less expensive than hospital maintenance, and a large proportion of the patients thus "placed out" make a lasting and happy adjustment to their surroundings But these ends cannot be attained unless those responsible for psychiatric services also provide the means, which include the allocation of a considerable special fund on which the costs will be borne, and the employment of a number of skilled social workers who are responsible for selecting and supervising the foster families In New York it has become plain that one social worker can supervise about 60 family-care cases, but if she has a heavier load than this there are more failures among the patients she places, they have to come back to the hospital, or another family has to be found for them. Miss Crutcher gives the exact budget that has been necessary, and she shows that, when every charge upon the scheme has been included, it saves more than 300 dollars a year for each patient thus dealt with. There is no danger, however, that such an accounting might lead local authorities to resort to family care under conditions in which it could become an unguarded or inhumane way of dealing with the chronic insane at a lesser expense.

Miss Crutcher's book shows that family care can be an important form of treatment. In psychiatry socialisation is a primary therapeutic measure; and the case histories which she quotes demonstrate how much more beneficial life in a well-chosen foster family can be than life in a mental hospital, even for those who will never wholly recover their mental health. Throughout the book a spirit of respect for the individual is evident, though in the presentation of her theme she is studiously practical It is certain that a mental hospital which utilises family care and has an adequate staff of social workers for the purpose, not only increases its power to benefit the patients but thereby reminds its staff constantly how artificial institutional life really is, and demands of them a constant readiness to work towards the goal of a more normal and satisfying environment for their mentally ill patients.

INJURIES OF THE RECTUM

THE obstinate tendency of the perianal tissues to form fistulæ is commented on although not explained by Blaisdell[14] in an article on traumatic injuries of the rectum He points out that a penetrating wound in this area is potentially fistulous and that the best treatment is to saucerise it as much as the anatomy permits This prevents the formation not only of a chronic fistula but of resultant deep infection which, owing to the inadequate path of escape, may be forced into various surrounding tissues and planes to give widespread and even fatal trouble He condemns almost any suturing of such wounds, including suture of the anal sphincter, since this merely helps to bridge the superficial gap and so promotes the very conditon to be avoided The same unsatisfactory result is favoured by the collapsed state of the tissues in the area, which he compares to "the closed position of an accordeon" The anal sphincter and the natural apposition of buttocks and thighs compel this collapse, yet even so he points out that other wounds with their edges in close apposition usually heal, even if infection is present, and there is no clear explanation why these fail to do so He also condemns temporary colostomy on the score that the time-lag before it is effective is too great to prevent fistula formation, and certainly colostomy is no cure for a fistula once formed. It is not perhaps out of place to wonder in what category third-degree obstetric tears might be placed, for if carefully sutured and well nursed they heal without trouble

12 Ross C A Conway J F *Amer J Surg* 1943, 60, 386
13 Foster Home Care for Mental Patients Hester B Crutcher Oxford University Press Pp 199 11s 6d)

14 Blaisdell, P C *J Amer med Ass* 1945, 128, 559

INCORPORATED SOCIETY OF CHIROPODISTS—The autumn convention of the society will be held in London from Oct 4 to Oct 6 The lecturers will include Mr N C Lake, FRCS, who on Thursday, the 4th, at 3 PM, will speak on posture with particular relation to the legs and feet, and Mr J Stamm, FRCS, who on Friday, Oct 5, at 10 5 AM will discuss disabilities of the foot associated with the first metatarsal Both these lectures will be given at the Royal College of Nursing, Henrietta Street, W1 On Saturday, the 6th, at 10 30 AM, at the Zoological Society, Regent's Park, NW, Mr F Wood Jones, FRCS, FRS, will deliver a lecture on the evolution of the foot Further information may be had from the secretary of the society, 21, Cavendish Square, W1

Special Articles

FILING OF ABSTRACTS AND CASE-RECORDS

G W DUNCAN
FRCSE
SURGEON

H G HANLEY
MD LPOOL, FRCS
SURGEON

H J V MORTON, MD CAMB, DA
SENIOR ANÆSTHETIST

HILLINGDON COUNTY HOSPITAL

ATTENTION has been drawn to the application of a simple efficient punched card filing system for the recording and sorting of anæsthetic case-records[1] This system has been used for some years in various special departments at Hillingdon County Hospital as a means of filing and cross-indexing medical abstracts.

A card is provided ruled on both sides and measuring 6 in × 8 in. with room for about 400 words in writing[2] Holes punched round the edge are marked with the numbers 1–57, two alphabets and an extra set of vowels (fig 1) The holes can be cut into "Vs" with the simple instrument provided If a long needle is passed through any particular numbered hole in a pack of cards symmetrically aligned, and the pack is then lifted, cards cut at this number will drop out Thus a large number of cards can be rapidly sorted

Reference codes for special subjects have been devised As an example the code used when abstracting published work on anæsthetics is set out in full below As a further example, the method employed for genito-urinary literature is to use one alphabet on the card to indicate broad anatomical groups—e.g , B for bladder, K for kidney, &c The numbers refer to methods of investigation cystoscopy, pyelogram, &c , to specific operations, nephrectomy, cystotomy, resection, &c , and miscellaneous features, various symptoms, prognosis, antiseptics, &c An ample supply of letters and numbers on the cards allows of the construction of a classification to suit individual interest on any subject

THE SYSTEM IN USE

The title and reference are written on the top of the card The first letter of the first author's name (if there is more than one author) is marked on one alphabet, to facilitate location when only a reference is given. After the abstract of the article has been written the appropriate letters and numbers relating to the subject matter are marked The V-cutting can be done at some convenient later date

Examples from the anæsthetic code—

1 Experimental studies dealing with the action of various drugs—e g 'Pentothal' and cyclopropane—on the stomach would be marked: 10, 16, B, L, extra vowel A

2 Spinal anæsthesia sequelæ affecting the nervous system = 36, A, extra vowel I, and drugs concerned also marked

Cards of special present interest can be simply collected together, or alternatively grouped under one of the remaining unused letters P–Z Articles of great interest and available in the original, but too long to be abstracted satisfactorily in the space provided, can be recorded as a reference only, and the code numbers of the subject matter cut in the usual way

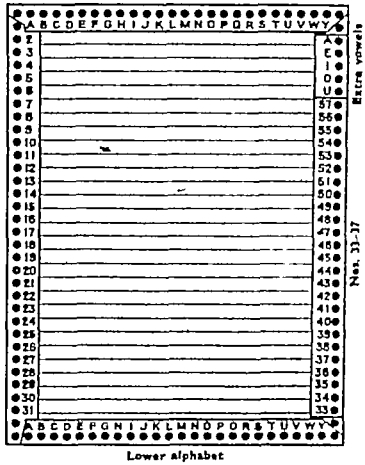

Fig 1.—Card used for filing medical abstracts.

Similar cards are used for keeping a private record of interesting cases which have been treated to a conclusion One alphabet is used for patients' names, the other for various organs. The numbers refer to pathological conditions, operative procedures, investigations, &c Thus it takes but a few moments to get out, for example, all cases of peptic ulcer for which partial gastrectomy was performed, the type of operation performed and the end-result, or all cases of prostatectomy done in two stages and the percentage of such cases admitted with retention (fig 2)

There are many advantages in being able to use one's own code, but it is wise to accumulate a considerable number of cards before a final arrangement of code numbers is adopted

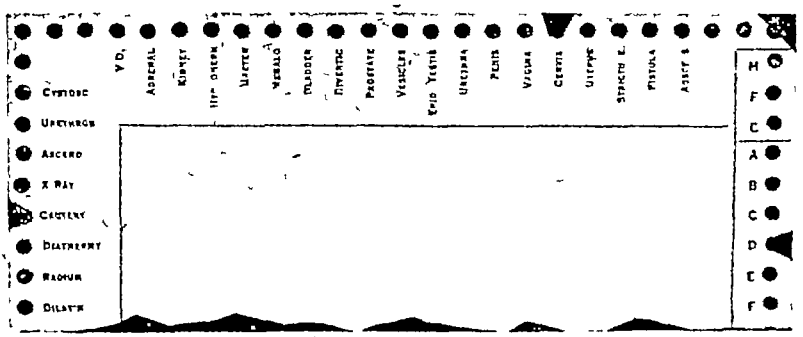

Fig 2.—Upper portion of card used for genito-urinary cases showing specimen Vs cut.

1 Nosworthy M D *Brit J Anæsth* 1943 18 160 See *Lancet* 1943 ii 50

2 The Copeland-Chatterson Paramount Card Obtainable from Copeland-Chatterson Co Ltd Stroud, Glos

The possibilities of this system will be apparent to the student of medical literature and to those concerned with keeping private case-records It may appeal especially to those deprived of easy access to large libraries and the *Index Medicus*, and to those who cannot enjoy the advantages provided by the more complicated cross-reference systems (e g , Hollerith) available in but a few of the larger centres. Perhaps the chief attractions are the opportunity for simple yet comprehensive cross-indexing and the facilities offered for ready reference to matters of particularly personal interest Thus the specimen " anæsthetic code " appended was designed for the personal use of an anæsthetist in relation to his own particular interests It is probably not comprehensive

ANÆSTHETIC LITERATURE SPECIMEN REFERENCE CODE

I. HYPNOTICS, ANÆSTHETICS, ANALGESICS, ETC

Liquids

1 Ether
2 Chloroform
3 Ethyl chloride
4 Divinyl ether
5 Trichlorethylene
6 Others (e g , paraldehyde, alcohol, cyclopropyl ethyl ether, &c)
7, 8

Gases

9 Nitrous oxide.
10 Cyclopropane
11 Other (e g , ethylene, propylene, &c.)
12, 13

Solids

14 Opiates
15 Bromethol
16 Ultra short acting barbiturates
17 Other barbiturates
18 Other (e g , chloral hydrate, &c)
19, 20

Local Agents

21 Cocaine, procaine, 'Nupercaine,' amethocaine, amylocaine, and their synonyms
22 Others (e g , 'Metycaine,' &c)
23

Other Substances of Importance

24 Oxygen (including oxygen lack, anoxia, &c)
25 Carbon dioxide (including CO_2 absorption, acapnia, &c)
26 Inert gases
27 Analeptics, BP raising drugs, vasoconstrictors
28 Atropine group
29 Others (e g , curare, magnesium sulphate, &c.)
30, 31

II METHODS AND TECHNIQUES

32 Intratracheal
33 Other inhalation methods (CO_2 absorption no 25)
34 Rectal
35 Intravenous
36 Subarachnoid
37 Extradural, peridural, splanchnic
38 Other regional methods
39 Infiltration
40 Surface application
41 Other methods (e g , refrigeration, electricity, &c)
42

III SPECIAL CATEGORIES

43 Shock
44 Toxicity, impurity, idiosyncrasy
45 Transfusion
46 Resuscitation, fatalities, emergencies
47 Explosions
48 Convulsions.
49 Apparatus and appliances
50. Analgesia
51. Preparation, premedication, basal anæsthesia
52 Choice, assessment of risk
53 Therapeutic and diagnostic use
54 Children and newborn.
55 Historical, general articles, organisation, teaching
56 Other (e g , signs of anæsthesia)
57

IV SYSTEMS (*lower alphabet*)

A. Nervous
B Digestive (dental, oral, and abdominal surgery included)
C Respiratory (thoracic, and nose and throat surgery included)
D Generative (obstetric).
E Urinary (GU surgery)
F Circulatory
G Metabolism Endocrine
H Locomotor and skin (orthopædic "traumatic," and plastic surgery)
I, J Blood Blood-chemistry

VI EXTRA VOWELS

A = Action of drugs on systems Condition of systems during anæsthesia or operation
E = Condition of systems before anæsthesia or operation
I = Condition of systems after anæsthesia or operation
O = Site of operation
U =

V GENERAL HEADINGS

K. Physiological studies
L Pharmacological studies
M Chemical studies
N Anatomical studies
O Theoretical considerations
P–Z for special use

VII AUTHOR S NAME (*upper alphabet*)

UNIVERSITY COLLEGE OF WALES, ABERYSTWYTH.—Mr W C Evans, PH D, at present biochemist to the inoculation department of St Mary s Hospital, London, has been appointed special lecturer in biochemistry in the department of animal health at the college

In England Now

A Running Commentary by Peripatetic Correspondents

I GATHER that the physicists concerned with research into atomic structure see little danger that the knowledge gained may be used in such a way as to detonate our planet. No doubt there are good reasons, beyond the understanding of those without special knowledge, for their confidence Nevertheless, I feel that we should be paying more attention to such eventualities, as well as to possible aberrations of the scientific workers—the human part of humanity's recording and interpreting apparatus.

The effort to escape responsibility is one of the most prominent features of human nature, and it is not to be expected that physicists are essentially different from all other human beings in this respect ; throughout recorded history technicians have been glad to use the facilities afforded by rulers to follow their calling, without responsible concern as to the way in which the fruits of their labour may be employed. So we can say with confidence that *if in fact* we were on the eve of a discovery which used as it would be used in existing conditions, would lead inevitably to the destruction of the world, the normal reaction of a scientist who had a glimpse of the possibility would be to say to himself .

" This is absurd. I'm getting rattled. How could the world come to an end ? I'm just an honest scientific worker doing a most exciting job of work, and my countrymen are relying upon me to get on with it I shall be letting them down if I allow myself to get neurotic about it After all I'm only one of a team, and my business is to discover the truth The use that other people may make of it is none of my business "

And that is probably very like what some at least of the atom-splitters have been saying to themselves lately. It is unlikely that any sane man is capable of believing fully that our world could come to a sudden end as the direct result of a simple discovery, made by himself in the ordinary course of his work ; or indeed that it could come to an end in the near future by any means whatsoever and such a disability to believe, being of emotional origin and supported by the similar attitude of his colleagues would be very little influenced by the actual presence and logical evidence of danger

One may at least hope that a committee of physicists not themselves directly concerned with atomic research has been set up to advise the Government continuously on the possibility of such risks arising as research proceeds, and that the public, better balanced emotionally than those specialised either for research or administration, will be kept continuously informed of its findings.

But even if man is still free for a while from direct responsibility for the preservation of his planet, he cannot any longer evade responsibility for the future of life upon its surface, and we do not need the report of any committee to tell us that this is in peril It is, after all, life that concerns us, and the sudden explosion of our planet would be no more than a merciful and timely end if the evolution of life upon its surface had ceased its upward striving, and had no possibility before it but slow disintegration and degradation It is some years since Julian Huxley wrote

" When civilisations and societies are organised so that their prime purpose is the pursuit of spiritual values, the life will have passed another critical point in its evolution as always, what has gone before is necessary as foundation for what is coming, and the biological conditions must be fulfilled before the new and higher edifice can be built but, as when the mammals superseded the reptiles, so a change of aim will mean the rise of a new type to be dominant and highest form of life

" This can only come about so far as man consciously attempts to make it come about His evolution up to the present can be summed up in one sentence—that, through his coming to possess reason, life in his person has become self-conscious, and evolution is handed over to be the trustee and director 'Nature' will no longer do the work unaided Nature—if by that we mean blind and unconscious forces—has, marvellously, produced man and consciousness ; they must carry on the task to new results which she alone can never reach "

Essays of a Biologist, Pelican edition, p

Since then events have occurred which some may interpret as a prelude to the regression of evolution, and the atomic bomb has arrived to bring the danger home to us It is clearly high time for those who, having some interest in biology, are really concerned for the future of life on the earth, to get together Unless we use ourselves for the creation of a higher living organism, we shall expend our creative ingenuity in the service of the mechanically inspired forces of mutual destruction

Personally, I believe that the new biological entity with which the hope of the future lies is a consciously created multimental organism, but that is another story

* * *

The soldier's return! I'm all complete except for the barrel-organ However carefully one trains oneself to expect the difficulties, it isn't the same thing The other night I was bawled at by a little man in the neediest bowler hat I have ever seen. It shone like an engine-driver's cap, and his complaint was that I brought my car in at 4 pm, and said I might have to take it out again at 7 "I can't do with you running in and out we got three lorries to get in yet I'm sick of it, that's what I am" That is the answer really From the garage I went to the butcher's queue, to the milkman who can't spare me any milk, to the laundry who can't take on new people, to the shoemaker who can't do any more repairs, and to the cleaner's who can't save my coupons by dyeing my khaki They want doctors, but not apparently in Harley Street rents are doubled and rooms can't be shared

Was it all worth while? The boredom, the irritation of incompetent direction, and obsessional blocking of projects by red tape (a much heavier burden this than blood and tears)? It was. To have shared, with men and women in the Services, the odd frustrations and occasional terrors of war, was an incomparably rich experience To have seen the sun setting off the North African coast, lighting the craziest vessels riding in placid waters like mother-of pearl, under a blue and apricot sky, or the cool of evening after a sticky day, with flocks of green parakeets fussing about their bedding down, tumbling in and out of very green trees, with the wall of Himalayas blue and solid behind them; early morning clouds in the monsoon, and the oily flop of tepid grey sea in the Persian Gulf, with the squat white buildings of Bahrein shimmering in the glazed heat—these make the background of an experience which could have been gained in no other way I have shared the misery of uncertainty and delay, and have myself impassively frustrated the endless ways in which men try to hurry their return to every street The bewildered POW ashamed of his emotional outbursts, the sterling ATS sergeant whose figure is her misfortune, the tough NCOs who like to plague the young soldier with irritating orders—what a remarkable variety of human sublimity and nonsense!

Worth it? I should say so, whatever the rude civilians do to us. Excuse me, is this the queue for the barrel-organs? Thank you, brother, for directing me further down the line

* * *

The Irish have a word for a patient who is not doing well: "He has disimproved" they say Nothing could more gently hint at sanguine hopes gone wrong disimproved is just the word for transport in London my day In my early childhood we had horses in variegated colours and the genial and winking men in rugs, who held the reins, would pull up the bus for any waving hand Then we had motor-buses, which, if less reliable than horse-flesh, were at least as willing to stop for the convenience of others as for their own After that things disimproved rapidly Buses became more trustworthy but less accommodating they would only pull up at given spots though these, fortunately, coincided with the exits of the Underground Also, buses bore large numbers back and front and also on the sides, so that if you were coming up a side-street you could see what bus routes crossed the top of it. Each bus carried an informative headboard, giving the main points on the route and those of us with good sight were saved a peck of time and trouble Acceleration was poor, so that you could be sure of stepping off comfortably while the driver was changing out of gear Underground it was just as pleasant—there were brisk lifts to swing you up and down, and jolly liftmen: well, most of them were jolly But now all that is changed Buses have a conspiracy of silence about where they are going Their headboards give meagre notice of a final destination, their numbers are small, and no longer to be seen on the sides (sometimes not even on the back), the stopping places are arranged to give us as long a walk as possible from the Underground, there is seldom any information about routes on the posts where we queue up—only numbers—and acceleration is much too good The final insult is the new bus whose automatic doors, shutting smugly in your face, were designed after careful thought to sour the liberal heart and make the traveller stamp, and look, like the wild ass Apart from everything else, bus drivers, once a sort of knights-errant who snatched old ladies from the gutter and wafted school-children home, are now a changed race intolerant of any interruption they pause chafing at fare stages, ignore request stops, and shake off the last clinging ants from their vessel's stern as they spring away on their secret journeys Underground we plod through endless tunnels or stand wedged on moving stairways like bottles on a factory belt. If we get into one of the few remaining lifts, a patronising voice from heaven, possibly St Peter's, adjures us to "Stand clear OF the gates Thanks to all these disimprovements I can no longer say, as I used to do in childhood, that to get to any point in London from any other point takes three-quarters of an hour: I now reckon on an hour and a lost temper That's progress.

* * *

We are all on tiptoe at the moment expecting our prisoners in from Siam The Americans beat us to it again and got some of theirs out the day before the Nip envoys got in here—apparently without any trouble at all And some of our pilots flying over there have seen them waving outside the cages. A great whip round is going on for comforts for them—clothes, cigarettes, &c.—and everyone will be all out to give them a real welcome on rather limited resources.

The morale of our chaps is good, and they are very reasonable in realising that their demobilisation will take a little time to organise and that ships don't grow on trees There is, very naturally I think, a feeling that the game is over and that the rest of their job is just a matter of holding the fort until the Regulars come along to take over from them But it will help to pass the time if we see new places. Malay, Java, Borneo, &c (they all hope Bali, of course, where the girls are "wondrous fair to behold," they hear) Good luck to them, anyhow: they deserve a break.

* * *

It is not possible to remove "class" by mere legislation Benefits at first limited to the few become in time available to the many; mass production of what you will places the luxuries of the rich within reach of all In one way or another we all try 'to keep up with the Joneses" My observation is that the Joneses decline to be kept up with Consider plus fours: at first confined to the golfers, they soon appeared on the limbs of errand boys; whereupon the golfers retaliated by reverting to flannel bags An *Evening News* cartoon depicts two miners discussing how they will fare when mines are nationalised: as civil servants, of course they will work in bowler and striped trousers But as fast as the workman discards his corduroys the public school boy's parent realises their hard wearing qualities and dresses his son accordingly When owner-trip of a sports car was held vulgar, and when a two-seater implied inability to afford a closed car, the moneyed man drove in his saloon Now that everyone owns imposing saloons, it is the demi-crème to own a sports car and breathe fresh air again Maids and shop assistants have elaborate 'white weddings,' while doctors get married unobtrusively in the course of the morning round And everybody now has letters after his name" I bought some lens this week and found my vendor was a Fellow! Yes. FSPBHR So the next more lies with us—a small plate (large visiting card size) and a simple 'Dr Jones

* * *

There is much to be said for the scarce She keeps one up to scratch.

Letters to the Editor

VITAMIN-B DEFICIENCY AND NERVOUS DISEASE

SIR,—In the interesting leader in your issue of Sept 8 the conception of a "biochemical" as opposed to a "histologically demonstrable" lesion is developed, and the reader might not unreasonably infer that this conception provides the complete solution of the problems involved in the pathogenesis of polyneuritis in general and of beriberi in particular.

Nevertheless, the physician familiar with the clinical and pathological phenomena common to all ætiological varieties of polyneuritis will appreciate that between these phenomena and the proposed "biochemical lesion" there is a complete gap in our knowledge that this conception does nothing to fill

It may well be that thiamine is a catalyst in the absence of which nerve-cell metabolism in the brain breaks down at the stage of pyruvic-acid formation, that this substance then accumulates, and that in these circumstances there may be a failure to develop the full energy of carbohydrate which impairs the functions of the cells in question

Of the three items of this hypothesis, the first two cannot accurately be called novel, while the last is purely speculative The notion of a breakdown in carbohydrate metabolism, when carbohydrates are taken without a due proportion of vitamin, is clearly implicit in the work of Braddon and Cooper, Funk, and other investigators of the period immediately preceding 1914 and summarising this evidence many years ago (*Quart J Med* 1918, 11, 320) I ventured to suggest that some intermediate product of this arrested metabolism might be toxic for the nervous system, and thus act as the immediate factor in the development of beriberi. It is only within the past decade that modern biochemists have tardily returned to this early conception—in part, but without proceeding to ask whether the pyruvate that is reported to be present in excess in the blood and cerebrospinal fluid of beriberi patients may not be the toxic metabolite in question But however this may be the "biochemical lesion" as postulated in your article is clearly inadequate to account for the fact that the signs and symptoms of beriberi, as of other ætiological varieties of polyneuritis, do not point to the nerve-cells of the brain as the seat of the relevant disorder of function, but point unequivocally to the peripheral nerve-fibres, that when lesions are histologically evident these also are predominant in these nerves, and that whatever the functional activity of nerve-cells in the brain, this is not reflected in the clinical picture as an integral part of it

Something more is required to connect these two wholly disparate findings the biochemical lesion in the brain on the one hand and the clinical signs and the lesions in peripheral nerves on the other, and until this "something more" has been found we cannot regard the problem of polyneuritis as solved

It is not correct to say, therefore, that "we can easily explain" the occurrence of polyneuritis in the acute fevers, pregnancy, thyrotoxicosis, and alcoholism Indeed, there is no conclusive evidence that there is a polyneuritis of thyrotoxicosis, while the rare polyneuritis of pregnancy is a product of so many obscure factors that we may not even say that it is related to pregnancy per se

Brilliant as it is, the history of modern biochemistry reveals a persistent tendency to oversimplify the problems of polyneuritis, a very imperfect understanding of the many aspects of this malady, and a lack of historical sense which is seen as a disregard of the brilliant researches of the early workers prior to 1914 with a failure to appreciate the valuable lessons their work reveals

The truth surely is that to tackle the problems of polyneuritis with reasonable hope of success demands a comprehensive understanding of all its aspects, for we cannot expect to elucidate the factors operative in the production of a human disease without a sound grasp of its natural history, its forms and variations and its pathology, and some competence to view all these on the general background of neuropathology No-one, today, can claim to have experience of the full range of the clinical and pathological manifestations of beriberi. Our only source of complete information is the vivid and complete account given by Hamilton Wright over forty years ago (*Stud Inst med Res. F.M S* 1903, 3). I submit that no-one unfamiliar either with the disease or with this unequalled description can pretend to understand this illness Divorced from this essential information, animal experiments inevitably wander from the realities of the problem they seek to solve

There is nothing new or revolutionary in this point of view It has been cogently urged upon us by Sir Thomas Lewis and Mr Wilfred Trotter in their plea for a clinical science which shall attack medical problems by all necessary methods, clinical and experimental, and is to be pursued by workers ready and able to assess the whole field of relevant evidence

There could not be a problem calling more urgently for this comprehensive attack than that provided by polyneuritis. Only in this way shall we escape the departmentalism of thought and effort that has for long kept us back from the successful elucidation of the pathogenesis of all forms of polyneuritis. Genius and industry have not been wanting in the attack upon this problem, but it cannot be denied that broadness of view and integration of thought and effort have not been present That this is so, a historical survey of the history of beriberi research from the beginning makes only too clear

One other comment upon the leader may be permitted There seems implicit in it the assumption that in thiamine we have a potent and reliable remedy for polyneuritis, even though in chronic cases the results may not be so "spectacular" owing to the presence of structural lesions that require time to heal It would be difficult to give a more misleading picture of the therapeutic situation Though I have sought it for over twenty years, I have yet to see the case of polyneuritis, acute or chronic, that gave a clear and striking response to the administration of the vitamin-B complex or of thiamine, in whatever dosage and by whatever In what we call febrile polyneuritis the ineffectiveness of these substances is quite painfully obvious, while I have never seen the severity or duration of a case of alcoholic polyneuritis mitigated by them This, surely, is the common experience of those who like evidence upon which to base conclusions In a controlled study of over 2 cases of polyneuritis in the Boston City Hospital, (*J Amer med Ass* 1941, 116, 1615) reports that thiamine administration was found to have no influence upon the behaviour or course of the malady. If, indeed, there be any conclusive evidence in a contrary sense, it is high time it was marshalled, and the medical profession presented with a body of documented and controlled observation, provided by workers in whose capacity to assess the progress of an organic nervous disease, its response to treatment, we may have confidence.

London, W1 F. M. R WALSHE

INDEPENDENT RESEARCH

SIR,—Stimulated by your leader and Prof F Twort's admirable letter, I put forward the following considerations In my view there are two grades of research . (1) the initiation of some original and fertile conception , and (2) the elaboration of the process required to make the new conception of practical value to man Examples of class (1) are Becquerel's discovery that electromagnetic waves emerge from pitchblende, Manson's hypothesis that malaria was insect-borne, Fleming's observation that the presence of a mould inhibited the growth of a coccal culture The genius that evolves such a conception is almost always an independent worker, untrammelled by superior control, that rarely he may be a member of some team

Once the great and original idea is enunciated, then comes the value and the need of team-work Thus the Curies and others elaborated Becquerel's discovery, Ross worked out Manson's idea ; and Florey and co-workers brought Fleming's original observation to fruition Like Twort, I think excessive control militate against class (1) research No team of men linked together could ever win the Derby

I have known of one who began research as a labour of love, and working freely and unpaid, with fac

wisely granted by a far-seeing institute director, made discovery after discovery Unfortunately his circumstances altered, and he required financial aid from a public research fund At first this was granted freely and without control, and did not seriously impede him But later on, when a scientific committee assumed control over his researches his originality was hampered, and it faded and failed The committee was an excellent one, most anxious to safeguard public funds; but the glamour was gone—the poet could write no more odes, the composer heard no more melodies

Can we not foster both grades of researchers—the individuals as well as the teamsters?

Stocking Pelham Herts. THOMAS LUMSDEN

THE PERFECT AP

SIR,—Dr George Day in his article of Sept 8 states that twenty years ago nobody bothered to explain how an artificial pneumothorax worked That it does work in certain cases is now well known, but precisely how it works is still not clearly understood What we can do at the present time is to observe when an AP works and when it does not work, and so establish definite indications and contra indications for its use It is only when all these facts are known that we shall be able to deduce the mechanics of the AP with any certainty

We consider that the Perfect or Ideal AP is the AP with no restraining adhesions in which there is no tension exerted by respiratory "pull" through any portion of the lung, but Dr Day's contention that a diseased lobe retracts into the position best suited to its healing is a *teleological explanation which we cannot accept*

We regret the use of the word "immobilise" in the statement that a Perfect AP immobilises the diseased zone of lung tissue, as if the air were acting as a plaster to "splint" a fractured limb An AP does, however, minimise movement of the affected lobe, thereby resting the diseased area as much as possible

When screening a patient who has an AP with no adhesions it is commonly observed that the diseased lobe moves but slightly, whereas the healthy lobe or lobes perform a wide respiratory excursion; but the statement that the healthy lobe performs the breathing of the entire hemithorax must be untrue It is well known, for instance, that when a closed internal pneumonolysis is being performed on a patient with a simultaneous bilateral AP such a patient is liable to be more stressed than one in whom the disease is unilateral

The "contraselective" AP, as shown in fig 3, with the diseased lobe adherent to the chest wall through pleural emphysis, is to be condemned, except in exceptional circumstances Those patients who have such an AP which is still continued are those in whom the great majority of serious pleural complications arise, and an early favourable result does not necessarily mean permanent control and arrest of the disease There are, of course, some cases in which an AP cannot be regarded as effective and in which thoracoplasty is contra indicated In a few of these cases where there are dense adhesions over the diseased lobe which do not permit of adhesion section the AP may be continued until such time as a thoracoplasty is practicable This is done at the serious risk of potential complications, such as an erosion which may become an empyema, unexpandable lung, and marked mediastinal distortion which may develop during a prolonged imperfect AP

The "striking clinical improvement" given by Dr Day as a reason for continuing with an ineffective AP is not in actual fact be due to this AP In the majority of cases bed-rest accompanies collapse therapy There is no certain way of knowing whether clinical improvement" is due to sanatorium bed rest or to the partial AP which does not relax the diseased area By and large, imperfect APs do far more harm than good It is quick to recognise the good, but do we recall the harm in assessing which APs to maintain and which to discontinue?

Symptomatic improvement alone should rarely be considered justification for continuing an otherwise ineffective AP, for it generally is impossible to determine whether the AP or bed rest has produced the improvement Furthermore any improvement of this sort is temporary and unless other treatment is employed a large percentage of these patients will eventually die of their disease It must never be forgotten that empyema may be a relatively late complication

Dr Day's disquisition on how the Perfect AP works is of great interest in itself, and it is not to discredit his provocative article that we conclude this letter with a reminder that such Perfect APs represent only a small proportion of all cases from which they are derived J S Whitney, reporting to the National Tuberculosis Association in 1938, stated that of all patients treated in 75 representative sanatoriums in 1933 more than two-thirds had *no surgical treatment, and only 18% had a* unilateral pneumothorax Amongst the medical and nursing professions, where minimal lesions are detected by routine radiography, Perfect APs may be common but they must be regarded as a specially selected group from which no deductions can be drawn as to the problem in the general population But let us hope that with the introduction of mass miniature radiography on a nation wide scale the percentage of early cases found will become even greater and the number of Perfect APs correspondingly increased In other words, early diagnosis and prompt treatment must be the aim of our future medical services until such time as the disease can be prevented.

G R W N LUNTZ,
S M HILTON
British Legion Sanatorium Preston Hall nr Maidstone Medical Officers

DEMOBILISATION OF MEDICAL STUDENTS

SIR,—When theological students and special categories of arts students are being demobilised under class B, it is surprising, to say the least, that no arrangements have been made for priority demobilisation of medical students who surrendered their reserved status voluntarily in the early stages of the war and joined the fighting Services, especially in the dark days of 1940 and 1941 These young men had begun their medical training before the outbreak of war, and might have continued quietly with their medical studies had they not felt strongly the temporary call to combative service at a critical period of their country's fortunes

One is told that the case of these medical students is similar to that of other students Such is obviously *not* the truth They are a small group, deserving special consideration for the sake of the profession as well as in recognition of their own patriotic zeal

London W1 WILLIAM BROWN

AGAR FOR LOCAL PENICILLIN THERAPY

SIR,—In their paper of June 9 (p 720), Coles, Barker, Robertson, and Cowan described a method for the preparation of 'Penagar' and claim various advantages for it While their criticism of our original penicillin agar is no doubt correct, it is to be regretted that they were not familiar with later papers (Modifications in Penicillin Agar Production, by Roberts, Murphy, and Jones, *J med Ass Fire*, October, 1944, p 41; Penicillin in the Treatment of Breast Abscess, by O'Hanlon and MacCluncy, *Ibid*, p 43) These papers give an account of a method for the production of 'Pen Agar' which permits the penicillin content to be controlled, and which is considered superior from the operational point of view It has been in continuous use since November, 1944, in the laboratories of a Dublin firm of manufacturing chemists

It is interesting to see that Coles et al confirm these earlier results—e g, refrigerator life of penagar rapid diffusion of penicillin, rapid healing if the organisms are penicillin-sensitive, and the necessity for "one dose per bottle"—in our case a standard of 20 c cm.

University College Dublin OLIVER ROBERTS.

SIR,—While in no way criticising the interesting work of Coles and his colleagues we feel it necessary to point out that '*Pen Agar*' is a term used by us to describe an identical product which has been manufactured by us since November, 1944, under Licence no 72, Therapeutic Substances Act Pen Agar since its introduction to the medical profession in this country has been advertised in the Irish medical and pharmaceutical press

Bachelor's Walk Dublin. P C CAMIS & CO LTD

RENAL ANOXIA OR HYPERSENSITIVITY?

SIR,—Professor Maegraith and his co-workers perform a valuable service in emphasising the clinical and pathological unity of a group of conditions of widely different ætiology, all characterised by renal changes, which they call the "renal anoxia syndrome" (*Lancet*, Sept. 8, p. 293) But renal anoxia may be only the proximate cause of the tissue change, and the emphasis they place on it may obscure the fact that many of the conditions have a characteristic generalised morphology suggesting a common pathogenesis In brief, they show vascular lesions, varying from œdema of the intima and media to a necrotising arteriolitis and phlebitis, associated with an interstitial œdema, exudation of erythrocytes, and infiltration with basophil macrophages, lymphocytes, plasma cells and occasionally eosinophils In the liver there is a separation of the endothelium of the sinusoids from the liver cells, and in severe cases fragmentation of the liver cords, with areas of focal necrosis and a periportal cellular infiltrate In the kidney there is a slight proliferation of Bowman's capsule, focal tubular degeneration with pigmented casts, and an interstitial cellular infiltration The spleen and lymph-nodes show a histiocytic proliferation with areas of necrosis Interstitial changes in other organs result in interstitial myocarditis, pneumonitis, pancreatitis, &c

E Clark and B I Kaplan were among the first to describe these morphological lesions in human serum-sickness (*Arch Path* 1937, **24**, 458), and A. R Rich observed them in association with periarteritis nodosa both in patients receiving serum treatment for pneumonia and in fatal sulphonamide reactions (*Bull Johns Hopk. Hosp* 1942, **71**, 123 and 375) B Black-Schaffer gave a detailed description of these generalised tissue changes in fatal sulphonamide reactions, and provided ample evidence that they are consequent on a generalised tissue hypersensitivity to a protein-conjugated sulphonamide with antigenic properties (*Arch Path* 1945, **39**, 301)

The incompatible blood-transfusion reaction is clearly a hypersensitivity phenomenon with an antibody reaction to a foreign antigen

In the infective group a detailed analysis of the lesions in scrub typhus and allied rickettsioses by A C Allen and S Spitz (*Amer J Path* 1945, **21**, 603) reveals that the lesions resemble those described above On the bases of these characteristic tissue changes these workers emphasise the importance of "an indirect, possibly toxic, but more probably hyperergic effect of the Rickettsiæ on the tissues" In Weil's disease and yellow fever, hepatic and renal lesions with focal necrosis and an interstitial exudate are the rule Recently cases of gas-gangrene surviving the initial "toxæmia" succumbed later with the "renal anoxia syndrome" and the same generalised histological picture. It should be noted that in both Weil's disease and gas-gangrene there is extensive muscle destruction.

Although the interpretation of histological changes in terms of allergy must arouse considerable scepticism, it nevertheless seems reasonable to suggest that in the crush syndrome. and in anuria following burns and retroplacental hæmorrhage, in which similar generalised tissue changes occur, some product of tissue destruction, either alone or conjugated with protein, may behave as an antigen and incite a hypersensitive tissue reaction

Maegraith includes in his review the renal changes in alkalosis and pernicious anæmia. Although these conditions are associated with renal anoxia, their clinical and morphological features are very different from those observed in other conditions showing the "renal anoxia syndrome"—The case of alkalosis described by N. G B McLetchie (*J Path Bact* 1943, **55**, 17), showing lesions reputedly similar to those of the crush syndrome, was not entirely convincing

If it be assumed as a hypothesis that the tissue changes in this group result from the fixation of an antibody in the tissue, and in certain individuals a hypersensitive reaction between this fixed antibody and a circulating antigen, then the members of the whole group fall naturally into a number of subdivisions —

(1) Organismal antigen rickettsial infections, yellow fever
(2) Infections associated with antigens derived from products of tissue destruction Weil's disease, gas-gangrene, septic abortion, and possibly blackwater fever
(3) Antigens derived from chemical compounds conjugated serum proteins sulphonamides, &c
(4) Antigens of the blood-groups ABO and Rh transfo reactions
(5) Antigens derived from the products of tissue breakdo traumatic uræmia, retroplacental hæmorrhage, burns

It is natural that the clinical features of these vari groups should be far from uniform, for the earlier ma festations of such diverse conditions will be modif profoundly by the direct effects of the different cau agents (e g , bacterial exotoxin) The renal lesion of t "renal anoxia syndrome" may, however, be the loc expression of a generalised hypersensitive tissue reactio of the immune-body type The fact that in some cas the preponderant lesion is renal has so concentrat attention on the kidney that the fundamental charact of the reaction has been overlooked

Such a concept may offer a rational explanation of t erratic occurrence of the syndrome in individuals expo to the same ætiological factors, and also suggest a n therapeutic approach to a symptom-complex of gr prognosis

Department of Pathology,
Radcliffe Infirmary, Oxford

ROSEMARY BIGGS.

BANTING MEMORIAL DIABETIC CONVALESCE HOME

SIR,—The debt of life and health that the diabe world owes to Banting's discovery of insulin is beyo words, and diabetics in this country want to recog it adequately by a practical memorial The Diabe Association, a combination of lay patients and interest doctors, is planning to honour his memory by establish a convalescent home, badly needed but so far n existent, where diabetics leaving hospitals after ac treatment can be fully restored to normal health proper diet, insulin, and diabetic training It will ser too, as a holiday home for diabetic children

This home must be started by voluntary effort have already collected £8000, but we aim at a w memorial and need £50,000 The people whose plea and duty it is to provide this money are ov diabetics, especially the rich, who know the bl of insulin for themselves or loved members of families It is difficult for us to get in touch with th and there could be no better means of contact the doctors who treat diabetics We therefore beg doctors to acquaint their diabetic patients of memorial scheme to Banting and to urge them to it handsomely. Subscribers should communicate our Association, at 9 Manchester Square, London, W1

R D LAWRENCE
Chairman, Diabetic Associati

DOMESTIC STAFF IN HOSPITAL

SIR,—As a ward sister I felt I must write to say how much I and my colleagues agree with the view that age of domestic staff is indirectly the cause of the shor of nurses

In the hospital from which I have recently resi the nursing staff were resigning at the rate of 10 month. The main grievance of student nurses was they found the work too hard—not because they had do too much nursing, but because they had most of domestic work to do, and had to skimp their nu treatment They never had time to stop to see treatment a doctor might be doing, and had no ho giving patients any individual attention They off duty late and dissatisfied, too tired to study or relax More ward sisters left this hospital in 6 m than I have seen leave other hospitals over several y again because of the acute shortage of domestic A ward sister with a ward of 30 patients and a ma staff of 3 nurses, and—if she is very lucky—a staff would have to wash up the patients' breakfast c when she came on duty in the morning This wa many domestic jobs that fell to her, because hardly in the hospital had its quota of domestic staff course her own work could not be neglected. sisters were thus too busy to teach the nurses an and the nurses never had time to be interested in went on.

I trained in an LCC hospital, and was half way through my training when war broke out I don't think I had to wash up after patients' meals 6 times during my training, and I never saw a nurse sweep a ward floor The system adopted by the LCC of using 2 orderlies to each ward, as well as a ward maid, could indeed be followed by other hospitals with advantage

I have asked a number of women whether they would work in hospital as domestics or orderlies; they say they would like the work and the hours, but point out that they can get 2s and 2s 6d. an hour elsewhere The solution seems to be more salary for domestic staff in hospital Incidentally, salary seems to be the least of the grumbles of the student nurse.

I wish the medical staff would become a little more interested in these problems The nursing care of their patients should be their concern, and if this is skimped they can't expect the desired results from the treatment

Leytonstone E M BATEMAN

HYPOPIESIA

SIR,—At times one is hard put to it to find the serviceable treatment for low blood pressure attended by symptoms, usually distinctive enough, if subjective In the adult, hypopiesia is taken to mean a systolic pressure of 110 mm Hg or less, with a diastolic pressure ranging below 70 mm Hg, this last may however, go undetermined because of the transitional sound being indistinct or inaudible. The disorder is physiological and symptomless in some, symptom producing in others, symptomatic of co-existing disease in others still.

The ambulant hypopietic, who comes complaining, is unconscious of an ailment he cannot define: he shows a disposition to fleeting hypotensive attacks the nature of which examination will bring to light The guiding symptoms consist in dizziness on change of posture to the upright, spells of weakness and tiredness with a *lessening of physical strength inability to stand about* beyond minutes without this inducing sweatings, yawning, nausea, and faintness throbbing pulsation in head and fingers synchronous with the pulse-beat, and the patient is introspective and neurasthenic

An oppressive hypotension, with symptoms such as these, is commoner in men than in women During the war years, the derangement was found to be not infrequent among those who were compelled to stand while at work The cause assigned was lowered vasomotor control with vascular stagnation in the splanchnic circulation excited or aggravated in attacks by some emotional or digestive upset

In treatment little beyond temporary benefit, if any, is to be had by the use of pressor drugs such as amphetamine sulphate, adrenaline, or ephedrine In practice, these chemicals are only a small part of the treatment, which, after all, should not consist in spasmodic attempts at raising pressure in terms of millimetres of mercury Whatever therapeutic method is employed, no speedy or persistent rise in pressure that is substantial is likely to happen furthermore, efforts aiming solely at buoying up to register rises in pressure by instrument are for the most part misdirected, and are apt to miscarry Reassurance enough rest with regular physical exercise, will help; but what I find affords greatest benefit is a firmly adjusted four inch or five inch abdominal web belt, with buckle fastening, worn over clothing at the level to give an uplift to the lower abdomen This, if need be, can be kept in position by a perineal thong This belt succeeds when nothing else will, and is usually declared by the sufferer to be a helpful, invigorating part of the treatment; so much so that he will by and by cling to the belt tenaciously and for long Even in the hypopietic who takes to the air, whether as pilot or passenger the abdominal belt so worn may obviate the symptoms excited by quick variations in height and pressure while flying and appears to me to be a necessary item of equipment for all airmen

Hypotensive attacks are transient and troublesome though neither morbid or mortal With the correcting concomitant disorder or disease the supporting belt seems to be the best remedy at present available, and invariably is accepted by the patient as being good and sufficient for his disability

Bournemouth S WATSON SMITH

BISMUTH COMPOUND IN ARTHRITIS

SIR,—Last year you published a communication from me announcing the use of sodium bismuthyl tartrate in arthritis (1944, i, 264) Although it has been in the *British Pharmacopeia* since 1936, its use had hitherto been confined to the treatment of yaws and syphilis.

The injection which appears in the *BP* is not entirely suitable for use in rheumatism, and a better and more stable solution has been made for me by Messrs C J Hewlett & Son Ltd Administered with the usual *aseptic precautions it should not produce any undue* local reaction Having used the drug now for several years, I have given some thousands of doses without any mishap, and have yet to meet with any toxic effects With increasing experience, however I have modified my technique of dosage I now rarely find it necessary to give more than half a grain in a single dose, or to repeat it in less than four weeks After a few doses this period can be extended to six weeks or two months, and, in a few of the more intractable cases where administration has to be continued for upwards of a year, I have found that a dose every three months is all that is required To exceed this dosage is to court failure It is of equal importance to inject the solution deeply into the muscles either of the gluteal region or of the thigh (through the fascia lata) A number of cases have been brought to my notice where these precautions have been neglected, with dire results Unfortunately in such cases it is almost always the drug that is blamed and not the user

Cases that have been treated unsuccessfully with gold *salts, because of their intolerance or their lack of* response should not be treated with this drug until all the gold has been eliminated This may take upwards of a year When gold has been used it is wise to commence with smaller doses and proceed slowly until responses are gained Bismuth, like gold, belongs to *the group of heavy metals and probably acts in a similar* manner But it has less toxic effects, and I regard it as superior to gold, both for this reason and because fewer doses need be given

I am often asked what is its precise action on the body and how it produces the results claimed A correct answer to this demands extensive laboratory investigation which I am not in a position to pursue; nor have I so far, been able to persuade anyone else to investigate Personally, I am quite content that its action should be regarded as empirical Numbers of our best known and successful remedies are

London W1 PERCY HALL

MEDICAL FILMS

SIR,—May I, from the student's point of view, suggest a programme of development?

The many films demonstrating surgical operations may be useful to postgraduate and research workers but not to the student, who needs little knowledge of operative surgery On the other hand films dealing with the diagnosis of "surgical" conditions, and the indications for operations are urgently required Films of "medical" conditions are also almost unobtainable This particularly applies to those presenting short case-histories, which need not contain controversial material

Having decided on the type of film required a long term and a short term policy, to operate simultaneously, are necessary The former would operate through a university grant for film making; this could be divided into two parts the larger fraction to be devoted to commissioning films requiring considerable technical resources (e g animation) by professional units and the smaller to making the non-controversial case-history type The latter could well be entrusted to the teachers and students of medical schools who are interested in film making The theory that only professionals can produce a good teaching film has recently been disproved by the private production of *An Introduction to Acute Infarmation* by three students (now qualified) of the Westminster Hospital With this example the formation of staff-student film units prepared to make films within a circumscribed area should not be difficult, if money is forthcoming

As an immediate step towards increasing the number of useful films available, a few thousand pounds would

be well spent in sending a purchasing commission, of perhaps six people, to the United States. This might consist of two members of the medical standing committee of the Scientific Film Association, two teachers, and (may I humbly suggest?) two students. From such a move we could expect a large and valuable stock of medical films in this country within a matter of months.

British Medical Students Association, BMA House, Tavistock Square, London, WC1. RICHARD R. L. PRYER, Acting Film Secretary.

LETTERS OF UNKNOWN ORIGIN.—We must remind correspondents that letters sent for publication under a pseudonym must always be accompanied by a note of the author's name and address. We have lately received several communications which cannot be published until we know their origin.—ED. L.

Public Health

Poliomyelitis among Campers

THE outbreak of poliomyelitis among a party of 130 Ilford scouts, who were in camp at Forest Row, Sussex, during the early days of August is so far limited to 8 cases. Dr. J. H. Weir, acting MOH for Ilford, reports that the boys returned from camp on Aug. 10, the first case being admitted to the Ilford Isolation Hospital on Aug. 19. The infection was severe, and the child died four days later despite the use of the Both respirator. Apart from this boy, 4 moderately severe and 2 mild cases, and 1 doubtful case have been admitted to hospital. All were members of the camping party except one girl, sister of a scout who had been at the camp but had himself shown no symptoms. The patients are progressing well, and the Both respirator gave considerable relief to one boy during the acute phase. As soon as the diagnosis of the first case was established, the Ministry of Health, the regional medical officer, the local authorities in Essex and Sussex, and the London Regional Scout Headquarters were informed, and all local doctors and hospitals were notified. Contacts were traced immediately and sanitary inspectors saw and advised them. Some of the camp equipment had been stored in a local church hall, and this has been disinfected by spray.

The outbreak serves to recall the part which flies are believed to take in the spread of infection (see *Lancet*, Sept. 1, p. 278). Camping sites, especially near farmyards, can be encouraging to flies. The Sussex camps, however, were isolated in the forest, not being close to the town or to any farmsteads. Flies seem to have been scarce rather than abundant, and the sanitary accommodation is said to have been well planned and properly looked after, under the supervision of the scoutmasters. Dr. G. K. Thornton, who attended the boys when they showed any indisposition, reports that 5 of them were in the sanatorium hut for one night on Aug. 6, one with bruises and 4 with slight temperatures and headaches. One of the 4 developed poliomyelitis on Aug. 13; the others are being followed up. No local cases have been reported near Forest Row, so far. The boys in the camps were at liberty to go where they pleased on one half-day a week—to visit the town and attend the cinema if they wished—but few of them took advantage of the opportunity; they preferred the attractions of the camp.

INFECTIOUS DISEASE IN ENGLAND AND WALES

WEEK ENDED SEPT. 8

Notifications.—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1151; whooping-cough, 1177; diphtheria, 423; paratyphoid, 12; typhoid, 12; measles (excluding rubella), 538; pneumonia (primary or influenzal), 268; puerperal pyrexia, 142; cerebrospinal fever, 25; poliomyelitis, 25; polio-encephalitis, 3; encephalitis lethargica, 2; dysentery, 278; ophthalmia neonatorum, 74. No case of cholera or typhus was notified during the week.

The number of service and civilian sick in the Infectious Hospitals of the London County Council on Sept. 5 was 947. During the previous week the following cases were admitted: scarlet fever, 65; diphtheria, 27; measles, 12; whooping-cough, 24.

Deaths.—In 126 great towns there were no deaths from measles, 1 (0) from an enteric fever, 1 (0) from scarlet fever, 7 (3) from whooping-cough, 14 (0) from diphtheria, 64 (9) from diarrhœa and enteritis under two years, 8 (2) from influenza. The figures in parentheses are those for London itself.

Newport, Mon., reported the fatal case of enteric fever. There were 4 deaths from diphtheria at Nottingham.

The number of stillbirths notified during the week was 182 (corresponding to a rate of 27 per thousand total births), including 18 in London.

On Active Service

AWARDS

CBE

Brigadier G. J. V. CROSBY, MD CAMB., RAMC.

DSO

Brigadier A. N. T. MENECES, CBE, MB LOND., RAMC.

OBE

Lieut.-Colonel E. J. CROWE, LRCPI, IMS.
Lieut.-Colonel J. M. MACF DREW, MRCS, IMS.
Lieut.-Colonel P. B. LONGDEN, MRCS, RAMC.
Lieut.-Colonel A. J. MARTIN, MRCS, RAMC.
Colonel M. S. PURVIS, MD GLASG., IMS.
Lieut.-Colonel C. E. ROBERTS, BM OXFD, RAMC.
Lieut.-Colonel R. N. TAIT SALL, MD LOND., RAMC.
Lieut.-Colonel JOHN WI FORD, Southern Rhod Medical Corps.
Colonel T. F. M. Woo MD DUBL., RAMC.
Lieut.-Colonel E. C. JAC RCAMC.
Lieut.-Colonel J. S. CANNEL, RCAMC.

MBE

Captain H. C. CAMPBELL, MB GLASG., RAMC.
Captain DHIAN SINGH, IAMC.
Major J. C. GREGORY, LMSSA, RAMC.
Lieut.-Colonel D. A. LANGHORNE, FRCSE, RAMC.
Major J. S. McCRAE, MB GLASG., RAMC.
Captain R. G. McWHINNEY, MB GLASG., RAMC.
Major C. F. VIEYRA, LM IMS.
Captain C. H. CONW RCAMC.
Major ROBERT FERGUS RCAMC.
Major W. S. GILCHR RCAMC.
Major C. C. HENNEB RCAMC.
Major W. M. G. WIL RCAMC.

MC

Captain G. K. BEATTY, MRCS, RAMC.
Captain T. A. TAYLOR, MB MANC., RAMC.
Captain JACK WEIR, MB GLASG., RAMC.

MENTIONED IN DESPATCHES

Surgeon Lieutenant J. A. COSH, RNVR.
Surgeon Lieutenant A. P. B. WAIND, DSC, RNVR.
Surgeon Lieutenant W. J. WINTHROP, RCNVR (posthumo

COMMENDED

Wing-Commander R. H. WINFIELD, DFC, AFC, MB.

Wing Commander Winfield was a member of the crew of RAF bomber *Aries* who in May made a successful flight over North Pole.

UNIVERSITY OF HEIDELBERG.—Dr. Karl Bauer, who has lately been appointed rector of the university, has been head of the department of surgery at Heidelberg since 1943. The town has suffered very little damage and the univer buildings are intact. It is hoped that the medical fa will reopen in October with about 1000 students, and month a start was made with ten-week refresher cours doctors from the Wehrmacht.

CHADWICK PUBLIC LECTURES.—The first lecture o autumn programme will be given at 26, Portland London, W1, on Tuesday, Oct. 2, at 2.30 PM, when Mr Russell, ARIBA, will speak on planning for new standards. Other lecturers will include Dr. W. P. K on health education (42, Broadway, SW1, Oct. 30, 2 Mr. F. C. Vokes, sewage disposal (90, Buckingham Road, SW1, Nov. 13, 2.30 PM), and Dr. A. M. H. Gra aspects of industrial dermatitis (Westminster medical school, 17, Horseferry Road, SW1, Nov. 29, 2. Further particulars may be had from the secretary trust, 204, Abbey House, Westminster, SW1.

Obituary

JOHN LOWNDES MOIR

M B-BANC

Dr J L. Moir, who died in the Manchester Royal Infirmary on July 24 at the age of 63, had been in practice at Congleton, Cheshire, for over twenty years before he retired in 1932 to his father's old home at Cemaes Bay in the Isle of Anglesey His retirement was full and happy, for it gave him leisure to develop former interests and explore new ones. In 1935 he was called to the bar at the Middle Temple, and this forensic recruit later contributed a paper on medical aspects of crime to the *Medico-Legal Review* As a speaker he was much in demand on the island, and many will remember his Armistice Sunday addresses at Cemaes church The work of the Red Cross and the Order of St John had always claimed much of his time, for he firmly believed in the importance of a widespread knowledge of first-aid in all sections of the community He thought that the Government should make a proficiency certificate in this *subject compulsory for school leavers and that it should* also be part of the medical student's training He urged doctors to take a greater interest in its teaching which he held should be definite, dogmatic, and up to-date, and for several years, with the help of carefully chosen collaborators, he had been preparing a book of fundamental first-aid "

On the outbreak of war he found he was too old to join the RAMC but he gave useful service as county medical officer and county civil defence officer for the British Red Cross Society, and he was also medical officer in charge of Gadlys Auxiliary Hospital at Cemaes Bay Perhaps his most important war work, however, was done as zone medical officer to the Anglesey Home Guard, in which he held the rank of lieut -colonel Here he found realistic scope for his enthusiasm for first aid, and in our columns with Mr Kelsey Fry he published a *method of treating a fractured jaw and with Air-*commodore H O Clarke a method of moving, where needs must, a patient with a fractured spine He also sponsored in his unit Colonel Duff's all purpose stretcher month before his death he was appointed the medical member of a pensions appeal tribunal

Dr Moir was educated at Charterhouse and the University of Manchester, where he graduated MB in 1908 After holding a house appointment at the Royal Infirmary he settled at Congleton in 1910, and in the following year he married Frances Parkin Their only son, now serving in the RNVR was named after her cousin, the late Lord Moynihan

Births, Marriages, and Deaths

BIRTHS

SMITH —On Sept 12 at Norwich the wife of Surgeon Commander H J Bennett RN—a son

EDWARDS —On Sept 10 at Woodford the wife of Dr Alan Edwards —a daughter

SCOTT —On Sept 8 in London the wife of Dr M Gilbert Scott—a son

BELL—On Sept 9 at Edinburgh the wife of Captain H M. Steel, RAMC (TA)—a daughter

TAYLOR —On Sept 8 in London to Dr Ruth Taylor (née Howitt) wife of Surgeon Lieut -Commander Selwyn Taylor RNVR—a son

BEST —On Sept 9 at Woking the wife of Surgeon Lieut -Commander W E Vivet RNVR—a daughter

MARRIAGES

COTE—FOSTER HARDAM.—On Sept 8 at Cambridge Stuart Bruce captain RAMC to Diana Joan Foster Harham

MURROW—KINCOSSON.—On Sept 8 in London Charles William Morrison Cameron MB to Joan Furze Kingcome

[illegible]E—WILLIAMS —On Sept 8 at Pwllheli Richard Lestrem Rees captain RAMC to Mair Wheldon

[illegible]LE—MOORE.—On Sept 8 in London John Wills captain RAMC to Anne Hamilton Moore

DEATHS

[illegible]ULL.—On Sept 9 at Cricieth Edward Cyril Doble MB BCh [illegible]

[illegible]SHIP.—On Sept 4 at Bournemouth Septimus Harold Fairrie MB VICT lieut.-colonel RAMC

[illegible]DAY —On Sept. 9 in Glasgow James Hendry, MD GLASG, [illegible] emeritus professor of midwifery in the University of Glasgow

[illegible]MANE.—On Sept 12 Gerald Quin Lennane MC FRCSI, FRCS formerly MO of Batterses aged 6

[illegible]MORY —On Sept 14 in London Isabella Lum den MB GLASG

[illegible]ENE.—On Sept 14 at Harrogate Ronald Cuthbert Orsone [illegible] MB OXON aged 58

[illegible].—On Sept 1 at Ketagiri 8 in Hs William Tarr, MD, FRCS [illegible] FRCSE, lieut -colonel DSO retd

Notes and News

WAR TIME NURSES

THE General Nursing Councils for England and Wales and for Scotland have agreed to grant a remission of 6 months in the training for State Registration to men and women who have had suitable nursing experience in the Forces or as members of the Civil Nursing Reserve the British Red Cross Society or the St John Ambulance Brigade Those who qualify for this remission will be able to enter for both parts of the preliminary examination after 6 months training Those seeking remission must

1 Produce evidence of not less than 2 years experience of hospital nursing under supervision of trained nurses and be recommended by the matron of the hospital in which they served

2 Enter for the first preliminary examination held after 6 months training (In Scotland they have the option of sitting part II of this examination—the theory and practice of nursing—before starting training)

3 Apply within 6 months of release from the Forces or the CNR or other nursing body to the hospital at which they wish to train

Remission can be claimed for appropriate experience acquired at any time since Sept 3, 1939

CHILD ADOPTION

CONTROL of undesirable societies and bodies for child adoption was strengthened by the 1939 Act which came into force in 1943, but private adoptions can still be arranged; and though in some cases the placing of the child may be undertaken carefully and conscientiously by responsible and trustworthy people, the system is obviously open to abuse At a joint conference, held in London on Sept 11 of the National Council of Social Service and the National Council for Maternity and Child Welfare, the National Children's Adoption Association, the National Adoption Society, and the Waifs and Strays Society defects in the existing law were thoroughly aired Speakers mentioned cases where, though the adoption was sanctioned by a court the adopting mother was a criminal or other undesirable person The child is examined medically, but no medical examination of the adopters is required by law Birmingham has voluntarily accepted the principle and several would be adopters have proved unsuitable on examination The adopting couples, too, need some measure of protection: they naturally like to take a child in infancy but in the early months of life it is often impossible to detect mental deficiency It was suggested that adopters might be spared the unexpected burden of a mentally defective child if the probationary period was longer Some of the faults of the present system it was felt, might be avoided if local welfare authorities had more powers of control, and if juvenile courts were more careful about granting adoption orders

INVITATION TO SANATORIUM NURSING

A PAMPHLET (*The Healing Touch*) originally compiled by the National Association for the Prevention of Tuberculosis, and now issued by the Ministry of Labour sets out the acute need for sanatorium nurses and appeals to nurses and other women to take up this branch of work. It is well written, and on the whole fair neither diminishing the drawbacks nor magnifying the compensations; but, like most pleas for nursing personnel today, it suffers from having to put a weak case The final appeal has to be to altruism: "Our Sanatoria are under staffed: they are in need of your help tuberculosis nursing is essential work. It is a big responsibility But you can take it

Some hints of easily remediable weaknesses in the present system find a place in these pages Feeling decidedly like pioneers, they put on their uniforms and set off on the first duty—a minor task, probably designed to give the recruit something to do on her first day But of course on her first day and for several succeeding days the recruit should have gone straight to the lecture room to be taught methodically and practically the technique of avoiding infection. Potential recruits may well wonder why experience precedes learning "The nurse properly trained in a modern sanatorium the pamphlet justly says is an all round competent person able to adapt herself mentally to any kind of nursing that the growing art of medicine requires" True; but how is the recruit to know what properly trained means or to recognise a modern sanatorium from its outside Until

we can guarantee that women entering to train as nurses, whether in sanatoriums or any other kind of hospital, will get good teaching, adequate protection from infection, and a reasonable private life, candidates will go on seeking other occupations, or will come into nursing only to give it up after a short trial A wastage in the region of 60% in the early years of training is a severe criticism of things as they are

A NEW JOURNAL

CLINICAL pathologists are known to be tenacious in overcoming difficulties, and they must have needed this quality to bring out a new journal just now The first number of the *Proceedings of the Association of Clinical Pathologists* is well printed on good paper with an austere, attractive cover in white and blue It contains six original articles and some excellent plates. Time and hard necessity will probably encourage the editors to pack the pictures more closely on their art paper, and never to leave one side of it blank, but otherwise they seem to have little to learn They expect to produce it irregularly for the present and not at any fixed intervals of time This journal has long been needed and will be welcome to many besides the group who have founded it We wish it long life

PRECAUTIONS AGAINST TYPHUS

To prevent the spread of typhus westward SHAEF established a sanitary cordon along the Rhine last March, and ordered that all civilians should be deloused before crossing it In addition, delousing was made a routine for all contacts of typhus patients, and for displaced persons and others who had been in Germany, Poland, and the Balkans, also for refugees and inmates of concentration camps, gaols, and other institutions A stockpile of more than a million pounds of DDT had been placed in readiness with plans for delousing some 18 million persons as soon as military operations permitted Brigadier-General James S Simmons, of the office of the Surgeon General at Washington, who gives this information, believes that the delousing programme "saved the European continent from the typhus scourge that raged through Europe following the first world war"

More than 2 million people have been immunised against typhus since the United States Typhus Commission went to Yugoslavia last January

A LEAFLET FOR WOMEN

A SENSIBLE, clear, and short account of menstruation for distribution at welfare centres, has been published on a blue leaflet by the National Baby Welfare Council, at the expense of Messrs John Knight Ltd It sets out the facts about normal menstruation in adolescence, after childbirth, and during the menopause, and gives useful advice about hygiene at the period Abnormalities are mentioned placidly, and even those which call for treatment are not discussed in a way to cause alarm The leaflet may be purchased at 1s 9d a dozen from the Council's offices at 29, Gordon Square, London, WC1.

Hospital Day in London

The annual street collection in aid of London's voluntary hospitals will be held this year on Oct 2 Collectors are urgently needed, and volunteers should offer their services to their nearest voluntary hospital or to Lord Luke, chairman, Hospitals Day, 36, Kingsway, WC2

Royal Sanitary Institute

On Saturday, Sept 29, at 10 45 AM, at the Southern Secondary School, Portsmouth, Dr I M. McLachlan will review the first year's working of mass radiography in the borough, and afterwards Surgeon Captain E C Holtom will speak on sanitation in the Navy.

Association of Industrial Medical Officers

The annual general meeting of the association will take place on Friday, Oct. 19, at the London School of Hygiene, Keppel Street, London, WC1, at 2 30 PM The speakers will include Dr J. C Bridge and Mr H E Griffiths A dinner will be held in the evening, and applications for tickets should be sent to Dr W. Blood, Cadby Hall, Kensington, W14.

Tropical Skin Diseases

It is stated that in tropical areas about 8% of all admissions to hospital from the United States Army are for skin disorders The good nutritional state of the American soldier, however, is believed to protect him from some of the skin diseases prevalent among natives of the tropics. "Tropical ulcer," for example, is rare in the U.S Army, though other forms of ulceration are common enough

Biochemical Society

A meeting will be held in the human nutrition resear unit of the Medical Research Council at the Natio Hospital, Queen Square, London, WC1, on Friday, Sept at 11 AM, when short communications and demonstrati will be given.

Medical Society of the LCC Service

There will be a clinical meeting of the society on Thurs Oct 4, at 3 PM, at Lewisham Hospital, SE13, when memb of the staffs of that hospital and of St Alfege's will demonstr cases

Return to Practice

It has been officially announced that Dr R R. TRAIL FRC has resumed civilian practice at 55, Harley Street, London, W1, and that Dr E L BARTLEMAN will resume practice at 58, Portland Place, W1, on Oct. 1

Royal Free Hospital

On Friday, Sept 28, at 3 PM, Lord Moran, FRCP, will deli the inaugural address at BMA House, Tavistock Squa London, WC1

Course for the DMR at Manchester

Candidates for the diploma in medical radiotherapy of t Royal Colleges are required to attend a course of systema instruction for 9 months and to spend a further 18 months the radiotherapeutic department of a recognised hosp To meet these requirements a course of lectures and practi demonstrations will begin at the Holt Radium Instit Manchester, early in January 1946, and it is hoped that afte wards paid posts will be found for candidates in radiothe peutic departments, where they may complete the attendan required Further information may be obtained from t dean of the medical school of the University of Manche Special consideration will be given to doctors who have b demobilised

A Domiciliary Consultant Service

The *Manchester Guardian* of Sept 14 reports that a r scheme has been introduced at Salford whereby a doctor m summon a specialist to the bedside of any of his child patie at the expense of the health department of the town. T only condition is that notice must first be given to Dr M garet Sproul, senior medical officer for maternity and c welfare, at the health offices, Regent Road, Salford Dr J Burn, the medical officer of health, has introduced t system because he fears that in working-class families doc are sometimes forced to take risks by ordering a child's remo to hospital, when gravely ill, as the only way of obtai specialist opinion

Catalogue of Scientific Films

The Scientific Films Committee of the Association Scientific Workers has now revised and printed its catalo of scientific films, which indicates their suitability for var types of audience The catalogue may be had for 2s 6d fr the Association at Hanover House, 73, High Holb London, WC1

Dr A H. G BURTON, medical officer of health for Ilf for 26 years, is retiring at the end of this month, and borough council are presenting him with a testimonial u seal recording their appreciation of his service

Major-General PAUL R HAWLEY, formerly chief surgeon the European Theatre of Operations, and Brigadier-Gen ELLIOTT C CUTLER, chief medical consultant with European Service of Supply, have temporarily joined staff of the Veterans Administration in Washington. Ge Hawley is medical adviser to the Administrator of Vete Affairs (General Omar Bradley), and General Cutl attached to his staff.

Appointments

CROUCH, MURIEL, MB LOND surgical registrar, Oster EMS Hospital, St Albans

HUGHES, PATRICK, MRCPI temp hon physician, Wermou District Hospital

MACDONALD, H A., FRCSE RSO, Great Yarmouth Hospital

NICHOL, R W, BA CAMB, MRCS, MRCOG temp obstetric gynæcologist, emergency maternity unit, Bradford-o Wilts

STAVELEY, DULCIE, MB LOND, DMRE part time ra Elizabeth Garrett Anderson Hospital, London

WEIR, J H, MD, B HY DURH act MOH for Ilford

LUMBAR PUNCTURE IN TREATMENT OF PENETRATING WOUNDS OF BRAIN

JOHN E A O'CONNELL, MB LOND, FRCS
NEURO-SURGEON, EMS

LUMBAR cerebrospinal fluid drainage is of undoubted value in the treatment of penetrating brain wounds Ascroft (1943) and Eden (1943) have both referred to it, without however discussing the subject Since no adequate reference to it has been found in the literature, it has been thought that a useful purpose might be served by a consideration of the indications for its use The work on which the opinions are based was carried out at an EMS neurosurgical unit and with a mobile neurosurgical team at a port hospital during the two months after June 6, 1944 Of over 1000 head injuries dealt with, more than 150 were penetrating brain wounds admitted in the acute stage The number of brain wounds is therefore small However since all the cases have been observed personally, most of them throughout the whole of their early treatment and many until their discharge from hospital, the observations may be worth recording The various indications for lumbar puncture in these cases will now be considered

POSTOPERATIVE USE TO REDUCE TENSION IN SCALP WOUNDS

Many penetrating wounds, treated early are closed by a strong two-layered suture of the scalp Here the suture line in the galea can be submitted to tension without risk of the scalp edges separating and a cerebral fungus forming, especially if the dural defect has also been closed In some extensive wounds however, the loss of scalp may be considerable, and the patient too ill for plastic procedures, the scalp wound may then be closed under tension Afterwards there will be anxiety lest the fluctuating tension of the underlying cerebral hernia should cause the suture line to break down If lumbar puncture is performed daily, the cerebral hernia is withdrawn inside the skull and the tension in the wound diminished, and with sound healing the risk of fungus formation passes, unless of course some intracranial infective complication should develop later

TO FACILITATE REMOVAL OF INTRACEREBRAL FOREIGN BODIES

When a missile enters the cerebrum an immediate rise in intracranial pressure will usually occur The existence of this hypertension is indicated by the presence of brain tissue in the superficial wound and by the sudden escape of blood clot and softened brain tissue which may take place when the dural opening is cleared during operation It is no doubt due to the presence of foreign bodies and blood clot in the brain at the site of injury and to local vasodilatation and œdema The intracranial hypertension is beneficial in that the cerebrum at the site of injury is forced into the dural opening and the subdural and subarachnoid spaces around the margins of the opening are occluded Adhesion between the membranes soon follows and the development of a meningeal infection is usually prevented thereby The raised intracranial pressure will however, handicap the surgeon at operation The tracks made by indriven metallic and bony particles are collapsed and it may be impossible to open up the depths of these tracks by retraction The use of irrigation and suction may overcome the difficulty, but there is a quite definite risk of removing viable cerebrum by the too energetic application of suction As evidence of this it may be stated that a monoplegia was converted into a hemiplegia in one patient of the series by the use of suction at reduced power (i e, a vacuum of 5–10 in. Hg) Since no large vessel had been injured during operation this occurrence can only be attributed to injury of viable brain by suction

In a small series of cases lumbar puncture was carried out after the patient had been anæsthetised and before operation It was found that the fall of intracranial pressure thus produced led to a dilatation of the track and its offshoots This facilitated exploration, and foreign bodies were removed more readily from what became a cavity rather than a track in the brain. Moreover, vigorous retraction and suction were found to be unnecessary

Preoperative lumbar puncture seems to be seldom required in patients who receive surgical treatment early It might be reserved for cases with deeply placed bone fragments or large missiles, for those explored later for bone chips overlooked at a previous operation, or for those cases—still not uncommon—in which a scalp wound is sutured over an unnoticed cerebral wound which later causes symptoms such as epilepsy In these cases the track is widely opened by the fall in intracranial pressure, any loose tissue can be removed by suction, and foreign bodies can be extracted with minimal trauma Figs 1 and 2 show the effects of lumbar puncture in such cases two examples of which follow:

CASE 1—An infantryman, aged 28 was admitted 36 hours after a penetrating left parietal gunshot wound After a short period of unconsciousness, he wakened to find his right side numb and weak He had a right hemiparesis and hemi hypoæsthesia, and a left parietal scalp wound from which brain exuded; X rays showed many indriven bone fragments With the patient under general anæsthesia, lumbar puncture was done and 40 c cm of bloodstained fluid withdrawn, reducing the pressure from 210 mm of cerebrospinal fluid to below 50 mm At operation a large cavity was found in the parietal lobe and a mass of bone chips was readily removed from it, together with blood clot and degenerate brain tissue. Penicillin was instilled through a tube inserted into the cavity by a stab wound and 10 days after operation the wound was soundly healed and the patient was evacuated

CASE 2.—A sailor, aged 20 received scalp lacerations from flying glass during an air raid He walked to hospital where a left parietal scalp laceration was sutured. Later he noticed weakness and numbness of his right arm, but it was only when he had a couple of epileptic attacks that a penetrating wound was suspected and he was referred for treatment His scalp wound was then healed and there were no abnormal neurological signs. Radiography showed indriven fragments of bone and glass, and the electroencephalogram a left parietal focus Three weeks after injury, with the patient under general anæsthesia lumbar puncture was done and the pressure reduced from 280 mm to 140 mm CSF; the fluid was clear A small left parietal osteoplastic craniotomy was carried out When the dura was reflected it was found that the wound track was widely open; it measured some 3 cm in diameter at the surface of the cerebrum and was 4 5 cm. long The loose tissue in the track was very delicate and the foreign bodies were readily picked out Since there was riding of the bone flap for some days, it is probable that some extradural bleeding occurred here

The wound healed soundly and the patient was returned to duty 2 months after operation

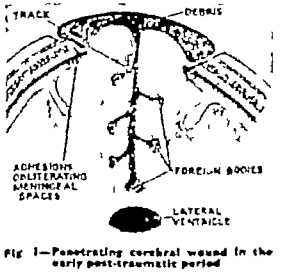

Fig 1—Penetrating cerebral wound in the early post-traumatic period

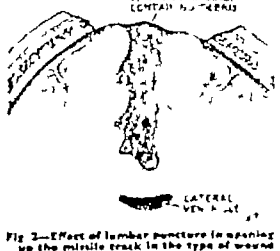

Fig 2—Effect of lumbar puncture in opening up the missile track in the type of wound shown in Fig 1

IN THE TREATMENT OF POST-TRAUMATIC CEREBRAL ABSCESS

When debridement of a cerebral wound has been inadequate, and especially when there are retained bone fragments, a cerebral abscess may form in some part of the track Unlike cerebral abscesses secondary to infection in the ear or nasal sinuses, these are connected, across sealed meningeal spaces, with the surface of the brain by the track—often a wide one—of the missile

In one group of such cases the patient after operation, develops pyrexia, symptoms of raised intracranial pressure and an inflammatory reaction in the CSF The scalp wound then breaks down, some pus is discharged, and a cerebral fungus develops, bearing on some part of its surface a sinus from which a little pus discharges (fig 3) This means that a cerebral abscess has formed and spontaneous drainage has occurred, but the drainage so established is seldom adequate, since the superficial part of the track collapses quickly and the abscess is likely to refill If lumbar puncture is done daily, or even less often, the fungus usually withdraws into the skull and the missile track opens, the abscess cavity can then drain freely and sometimes the responsible bone-fragment can be seen and removed If the track is too long for this, it may be possible to pass a drainage tube through it into the abscess cavity, which then gradually closes from its depths outwards In several patients with a history of this type treatment has been facilitated by lumbar puncture

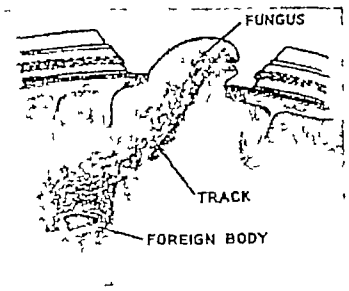

Fig 3—Untreated infected penetrating cerebral wound

Similarly, if an abscess forms after a longer interval, when the scalp wound is soundly healed, preoperative lumbar puncture will dilate the missile track, and when the scalp is incised gentle suction along the track reveals the abscess cavity, the cavity itself remains open after its contents have been removed (instead of collapsing as it would do if intracranial pressure had not been reduced), and contained foreign bodies can be readily seen and removed

Finally lumbar puncture may be of the greatest value in the postoperative management of a cerebral abscess Jefferson (1943) has stressed this After a brain abscess has been drained there is a constant tendency for the cavity to collapse This is probably due to both intracranial hypertension and local ventricular dilatation Cerebral tissue is forced into the dural opening to form a fungus plugging it and pus is retained in the deeper cavity Here lumbar puncture will widely open the cavity and allow of inspection of its wall and the removal of sloughs

At the termination of each lumbar puncture a sheet of thin rubber tissue is introduced into the cavity and packed in place with ribbon gauze (fig 4) Free drainage to the exterior then occurs between the waterproof tampon and the surrounding brain The following case-history illustrates several of these points

CASE 3 —A paratrooper, aged 21, was admitted 3 days after receiving a penetrating right parietal gunshot wound He had lost consciousness for a short time He was restless and looked ill and had a foul smelling right parietovertical brain fungus There was a left hemiplegia and cortical hemianæsthesia and paralysis of the right leg with cortical sensory loss X rays revealed a shower of bone fragments along the right side of the falx The wound was excised in the usual way, but no search was made for the deep bone fragments owing to his poor general condition The scalp defect was closed by mobilising scalp flaps and leaving an area of pericranium some distance from the skull defect to granulate Penicillin solution was instilled locally for 7 days The wound healed by first intention and the bare area rapidly epithelialised Twelve days later his condition deteriorated, there was high fever, and the CSF was under increased pressure and turbid, with a white-cell count of 48,000 per c.mm Three weeks after the first operation he was anæsthetised and lumbar puncture performed, intracranial pressure being reduced from 250 mm to 10 mm CSF The wound was then opened and the track was found to have been widely dilated by the puncture Gentle suction removed the delicate tissue which filled it and a large abscess cavity was entered Pus (*Staphylococcus aureus*) and many bone fragments—some loose and others adherent to the wall—were removed Though the bottom of the cavity was 10 cm from the surface, it showed no tendency to collapse Rubber sheeting was used for drainage and lumbar puncture was repeated almost daily After 16 days, pyrexia recurred and the CSF again showed a high pleocytosis A spreading encephalitis seemed to be present and the abscess cavity increased in size in front and below, with secondary hæmorrhage on one occasion Routine dressings and lumbar punctures were continued, and penicillin was given intramuscularly He improved slowly Four weeks later he was evacuated to another neurosurgical unit where the same treatment was continued When he was discharged 4 months after being wounded his general condition was excellent, there had been slight functional recovery, and his wound was soundly healed

IN UNTREATED WOUNDS SEEN AFTER INFECTION IS ESTABLISHED

It sometimes happens that a patient with a penetrating cerebral wound, who has been thought to be certain to die and has therefore not been treated by early surgery, survives his injury By the time improvement in his condition is manifest, infection in his wound is firmly established The therapeutic problem here is quite distinct from that of the penetrating wound seen early In the latter type of case one is dealing usually with bacterial contamination, the tissues have not been invaded and the local inflammatory reaction is minimal Here the complete removal of all contaminated tissue should allow of closure of the wound and primary healing In the wound first seen a week or more after injury infection is established Pus will cover the wound, granulation tissue will have formed in it and a barrier will have been set up in the tissues against the further spread of infection To debride such a wound adequately, if it were technically possible, one would have to excise a wide area of normal scalp, skull, and brain This would inflict unnecessarily severe trauma on the brain and would not even then ensure complete removal of infection and speedy healing Moreover, destruction of tissue barriers would increase the risk of spread of infection

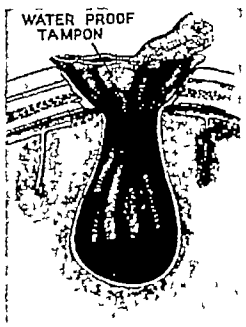

Fig 4—Effect of repeated lumbar punctures in opening up the missile track in the type of wound shown in fig 1 Note waterproof tampon method of dressing

It is believed that in the treatment of such infected wounds which are first seen a week or more after injury it is important to bear in mind the fact that infection has been localised by tissue reaction in the wound Healing by granulation should therefore be allowed to take place The difficulty arises, however, that fungation of cerebrum into the dural defect will close the superficial part of the wound track and retention of pus and foreign bodies will therefore occur Lumbar puncture performed daily, or more frequently, will convert the track into a smooth walled brain cavity from which sloughs and foreign bodies may be removed The opening up of the track and its offshoots can be further aided by gently wiping its walls with moist cotton pledgets The rubber tampon type of dressing will again be used here, as in the treatment of post-traumatic abscess. In due course the cavity is obliterated by the rise of its fundus to the dural level, doubtless owing to dilatation of the underlying lateral ventricle The granulating area then epithelialises Removal of marginal sequestra of the skull may be required but is not urgent. Thus, as in the case of post-traumatic abscess, the essential feature of treatment is the maintenance of drainage

Fig 5

5—Gunshot wound of left parietal region. Anteroposterior pneumoencephalogram 8 weeks after injury The portion of the left lateral ventricle related to the missile track is greatly dilated.

6—Left lateral view of the same case

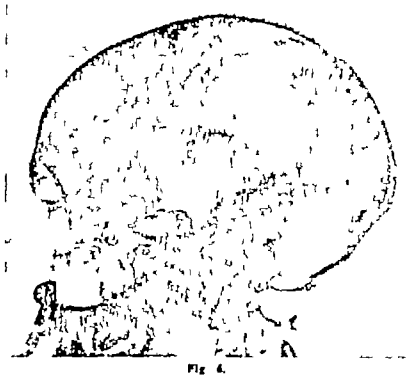

Fig 6.

from the depths of the track by opening it by means of lumbar puncture This treatment offers a needed alternative to operation in the cases which come late for treatment and in which the wound is of considerable superficial extent In untreated penetrations which have small superficial wounds, the latter will probably have healed spontaneously and the problem will be the different one of removing retained foreign bodies or of draining an abscess

CASE 4 —A sapper was wounded in the left side of his head by a shell fragment He was unconscious for several days, and then developed high fever and signs of meningitis and basal pneumonia When first seen, 9 days after being wounded, he had had no local treatment There was a wide scalp defect, much denuded skull, and through the dural opening a small brain fungus protruded, bathed in pus. He had severe dysphasia of mixed expressive and receptive type, and a right hemiplegia His general condition was extremely bad, with pyrexia, tachycardia and sacral decubitus The local treatment adopted was conservative, daily dressings being facilitated by lumbar puncture which reduced the small fungus and opened first the mouth and later the depths of the wound track Small collections of pus, foreign bodies, and sloughs were removed and the clean brain cavity was dusted with penicillin powder and dressed by rubber tampon After the man's transfer to another hospital 6 weeks later, his wound healed slowly though the functional defect remained severe

IN TREATMENT OF PROGRESSIVE CEREBRAL FUNGATION

The term cerebral fungus denotes a protrusion of the cerebrum through a defect in its covering scalp, skull and meninges. The most obvious cause of such a protrusion is an increase in intracranial pressure and several examples of fungation due to this cause may be mentioned The protrusion of cerebrum into the scalp wound at the time of wounding is one and that which is seen in the wound which breaks down post-operatively owing to retained infection another In cases of virulent infection with anaerobic organisms rapidly enlarging soft reddish brown fungus may develop within a short period of wounding In these examples the fungus is of but secondary importance but it is believed that there is a group of cases in which the presence of the fungus is the essential pathological and therapeutic problem When there has occurred a wide injury to the coverings of the brain and when the scalp wound remains unhealed there is a tendency towards progressive protrusion of cerebral tissue through the dural defect In such a case no underlying infective complication may be demonstrable and indeed intracranial pressure may be within normal limits This type of cerebral fungation has been discussed in a previous communication (1943a) and the hypothesis has been put forward that it arises and progresses because of the giving way of the wall of the lateral ventricle at the site of injury before the rhythmic pressure variations which occur within the lateral ventricle In another paper (1943b) it has been shown that the variations in intraventricular pressure with cardiac and respiratory activity are of considerably greater magnitude than is often realised It is believed that these pressure variations are important in the production of the localised ventricular dilatations which occur when an area of cerebrum of sufficient extent is injured When in relation to the injured brain a large defect in the cerebral coverings is present, the thinned and unsupported ventricular wall continues to stretch before the pressure thrusts to which it is subject It is therefore carried through the dural defect and a progressively enlarging cerebral fungus results If this view as to the aetiology of progressive cerebral fungation is correct entailing as it does an evagination of the wound track, the process may perhaps be regarded as a defensive mechanism which exteriorises the missile track

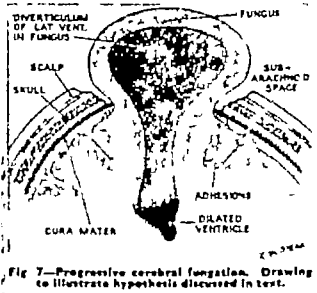

Fig 7—Progressive cerebral fungation. Drawing to illustrate hypothesis discussed in text.

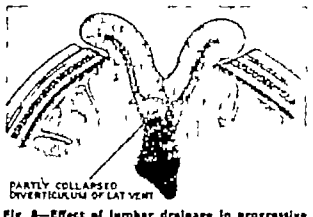

Fig 8—Effect of lumbar drainage in progressive cerebral fungation.

The pneumoencephalograms (figs 5 and 6) from the following case support this hypothesis

CASE 5.—A young sailor received a penetrating gun shot wound in the left vertex. He was first seen 7 weeks later, a primary operation having been performed elsewhere At this time there was a brain fungus 1 cm in diameter at the centre of an otherwise healed scalp wound Pneumoencephalograms made at the time of his illness show great dilatation of that part of the left lateral ventricle adjacent to the missile track. Had it not been for sound healing of the greater part

of his scalp wound the ventricular dilatation would probably have increased further, causing progressive cerebral fungation

Cases of this kind which have been treated by repeated lumbar drainage have done well The injured area of cerebrum becomes converted into granulation tissue and epithelialisation follows. In figs 7 and 8 this hypothesis concerning the ætiology of cerebral fungation and the beneficial effect of lumbar puncture are illustrated.

DISCUSSION

In the management of a patient with a cerebral abscess, an untreated infected brain wound, or progressive cerebral fungation, lumbar puncture must be performed repeatedly over a long period Puncture twice daily might be ideal, but the patient should probably be spared such an ordeal The cerebrospinal fluid pressure must therefore be reduced to a low figure—even to zero. If the drainage is carried out slowly over some hours, headache may be lessened. In some cases headache has been severe enough to call for intravenous anæsthesia By keeping the patient's head up and controlling his intake of fluid, it seems possible to delay the filling of the ventricles after puncture; and this makes a 24-hour interval between punctures permissible Continuous CSF drainage was established in one case by means of a ureteric catheter in the lateral ventricle, but it was slow, and lumbar puncture was necessary in addition before fungation was controlled It was considered unwise to use a wider catheter over a long period because of the risk of infection

The dangers of lumbar puncture in the presence of high intracranial pressure are now generally recognised In cases of brain tumour the hypertension may have given rise to a tentorial or foraminal pressure cone the size of which may be rapidly increased by lumbar puncture, so that fatal compression of the brain-stem is brought about. In many clinics lumbar puncture is therefore avoided in patients suspected of harbouring brain tumours The intracranial pressure after an uncomplicated penetrating wound is rarely, if ever, raised to the high level associated with, say, a posterior fossa tumour, and preoperative lumbar puncture probably carries no risk of causing a pressure cone In post-traumatic abscess, however, intracranial pressure may be much raised, and here preoperative CSF drainage must be slow, and only attempted with the patient anæsthetised and on the operating table If he shows respiratory embarrassment, the drainage must be discontinued at once, and operation begun.

The increase in intracranial pressure after wounding helps to arrest hæmorrhage along the track of the missile, and lumbar puncture may therefore favour bleeding Attention should be directed to hæmostasis in such cases One patient on whom a preoperative puncture was done died in coma 12 hours later, and at autopsy was found to have a large hæmatoma in the cerebrum in the neighbourhood of his wound Since the wound was associated with much destruction of cerebral tissue the hæmorrhage cannot with certainty be attributed to the puncture, but this must certainly fall under suspicion When a preoperative puncture is thought to be indicated in cases of this type, it might be wise not to reduce the pressure to below 100 mm of CSF

Since material lying in the superficial part of the wound will be withdrawn into its depths when the track is opened, the possibility that lumbar puncture may promote infection must be considered. If debridement is thorough at the outset, it does not seem that puncture could be responsible for any infective complication which might follow The meningeal spaces around the track of the missile are sealed early, and it is unlikely that infection could be drawn into them If it is thought that the wound may enter a lateral ventricle, the risk of aspirating infected material into the ventricle would certainly contra-indicate preoperative lumbar puncture

Finally, lumbar puncture can of course be used for the administration of penicillin in the treatment or prophylaxis of meningitis, and it will provide assistance in diagnosis

SUMMARY

Indications for lumbar cerebrospinal fluid drainage in the treatment of penetrating cerebral wounds are discussed

Preoperative lumbar puncture may facilitate debridement or the evacuation of an abscess, and may reduce operative trauma to the brain Postoperatively lumbar puncture may help to protect the scalp suture-line from tension

It has proved valuable in ensuring drainage in the wound which becomes infected and breaks down after operation, or in the late untreated wound first seen with infection established.

It is the essential part of the treatment of progressive cerebral fungation

It is of course useful for prophylactic or therapeutic administration of penicillin, and may also help in diagnosis.

I must record my debt to those whose assistance made these observations possible to Mr J P Haile, who shared in the management of many of the patients, to Mr. C Sanden, anæsthetist to our mobile unit, who kept duplicate records of our cases, and to those who kept us informed of the progress of patients after evacuation, especially Prof Geoffrey Jefferson and Lieut -Colonel E H. Botterell, RCAMC The counsel of Prof Paterson Ross has been always available and helpful

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TSUTSUGAMUSHI FEVER
ON THE INDIA-BURMA BORDER

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IT is now nearly thirty years since Megaw (1917) described his personal experiences of a typhus-like fever in India Since then small groups of cases have been reported, and Boyd in 1935 described 110 cases occurring among military personnel during the previous year On the results of *Proteus* strain agglutination he divided these cases into three groups, one of which comprised 35 cases agglutinating only the XK strain In 1944, Bardhan reported 41 cases of XK typhus in Lansdown and Jhansi, and Sen Gupta a single case in Calcutta

In Malaya Fletcher and Lesslar (1925), and Fletcher and Field (1927) described cases of rural typhus and of "tsutsugamushi fever," basing the distinction on the presence of a primary dermal lesion and bubo in the latter disease Anigstein (1933) maintained this distinction in reporting 90 cases of rural typhus in Malaya Lewthwaite and Savoor (1940), in a comprehensive survey of 250 cases of rural or scrub typhus (XK) in Malaya, and, as the result of cross-immunity experiments, demonstrated the identity of this disease with "tsutsugamushi fever"

This paper is based on a clinical analysis of 500 cases of XK typhus seen during 1943 and early 1944; a further 500 cases seen during the latter part of 1944 and in January, 1945, are included in the analysis of mortality and complications

EPIDEMIOLOGY

From Japanese and other publications we know that endemic areas of "tsutsugamushi fever" are often small and scattered and are usually in regions which have at some time been cultivated Nagayo (1923), writing of the "trombicula akamushi," says "as these various mites inhabit some small circumscribed areas, which are called 'yudokuchi' (literally poisonous place) and are usually very fertile, people, mostly farmers, are attacked by the mites only when they enter these endemic regions."

In the course of recent operations on the India-Burma border a large number of troops have been living and fighting in an area which before the war was little known and was rarely penetrated by outsiders The central section of this front runs through hilly country, areas which have at some time been under cultivation, but which have in many cases relapsed into secondary scrub jungle Thus it was not surprising that cases of XK typhus occurred sporadically among military personnel During the first nine months of 1943 only such cases were admitted to the medical division of a military hospital in Manipur State, but in October

November, and December, 1943, the disease became common, the epidemic subsiding in January, 1944. During the monsoon period of 1944 (June–October) and through the cold weather (November–February) there

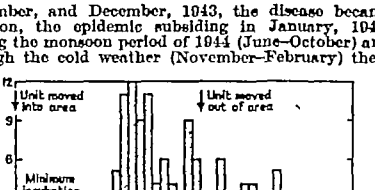

Fig 1—Daily incidence of XK typhus in British battalion entering endemic area.

was a further rise in incidence. Although the peak periods occurred during the late monsoon and post-monsoon seasons in each year, they also coincided with active military operations, in the course of which many troops lived and fought in these areas of scrub jungle.

The experience of one unit may be cited to illustrate how a hyperendemic focus may be restricted to a very small area and also to afford data on the incubation period.

A British battalion arrived on Oct. 11, 1943, from a non-endemic area. They camped at the foot of three small scrub-covered hills, and carried out training exercises there until they were moved out of the area on Nov. 2. As a result of this short stay there were 121 cases of XK typhus in the unit: the first occurred nine days after arrival and the last seventeen days after leaving the area. Fig. 1 shows the day by-day incidence. Other units in the vicinity had a few cases during the same period but no explosive outbreak of this type.

The only evidence as to the insect vector is negative in character—there was no infestation by body lice or fleas, and no history of tick-bites, in any of the 1000 cases.

CLINICAL FINDINGS

The clinical features reported from Japan, Malaya, and India are compared in table I with those of the present series.

TABLE I—CLINICAL FEATURES OF TSUTSUGAMUSHI AS REPORTED FROM VARIOUS LOCALITIES

	Japan (Nagayo 1923)	Malaya (Lewth waite and Savoor 1940)	India (Boyd 1935)	India (Bardhan 1944)	India Burma 1943–44
No. of cases		260 (15 Eur.)	35 (*1 Eur.)	41	500 (200 Eur.)
Primary ulcer	Usual	5%	Nil	Nil	11%
Rash	Usual	All Eur. Some Ind.	16/21 Eur. 1/14 Ind.	Nil	64% Eur. 31% Ind.
Adenopathy	Usual	40%	Nil	Nil	92%
Splenomegaly	Most cases	80%	Nil	Usual	47%
Deafness	Common	66%	Nil	Nil	35%
Pharyngitis	Nil	Often	Nil	Usual	34%
Conjunctival injection	Nil	40%	Usual	Usual	76%
Chest signs	Frequent	80%	9/35	40%	68%
Mental changes	Severe	35%	Common	All	100%
Flushing and cyanosis	Nil	2/15 Eur.	Usual	Nil	100%
Headache	All	92%	All	All	100%
Secondary fever	Nil	Nil	Nil	Nil	15%
Duration of fever	2–3 weeks	12–15 days	14·2 days	12–14 days	18 days
Case-fatality rate	30–60%	15%	Nil	Nil	6%

Eur. = Europeans. Ind. = Indians.

The *onset* is sudden in most cases. In 4 patients admitted to hospital for other causes, and who subsequently developed typhus, a fever of 103° F. was reached within 48 hours. Headache may precede the fever by a few days.

Primary ulcer.—The only cases included in the 11% were those showing a lesion with a black scab, which on separating left a shallow ulcer, and who also showed a primary regional adenitis. Men who have been living under jungle conditions usually show small skin abrasions, particularly on the legs, and these may well have included many primary bites in the abortive phases described by Lewthwaite and Savoor (1940). The distribution of the 56 eschars was: trunk 40, arm 0, leg 6, and neck 1.

Rash.—Seen in 64% of Europeans and in 31% of Indians. The onset averaged the third day, fading on the eleventh day. As a rule it was a blotchy pinkish brown macular or papular rash, fading on pressure; occasionally it was purpuric with persistent staining. When scanty it was found only on the trunk and was most definite over the pressure areas. When *profuse the limbs and face were also affected. It was equally* distributed on the flexor and extensor surfaces. In Europeans half showed a purely macular rash. Since a macular rash is difficult to detect on a pigmented skin this probably explains the varying incidence in Europeans and Indians.

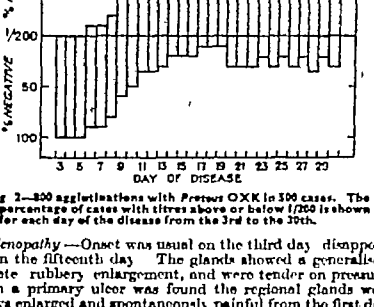

Fig 2—800 agglutinations with *Proteus* OXK in 500 cases. The percentage of cases with titres above or below 1/200 is shown for each day of the disease from the 3rd to the 30th.

Adenopathy.—Onset was usual on the third day, disappearing on the fifteenth day. The glands showed a generalised, discrete rubbery enlargement, and were tender on pressure. When a primary ulcer was found the regional glands were always enlarged and spontaneously painful from the first day. Even in the absence of a primary sore a primary bubo was often found.

Splenomegaly.—In 47% of cases there was an increasing enlargement of the spleen during the second and third weeks.

Deafness.—35% showed a nerve deafness, variable in degree and persistence, but usually improving during convalescence.

Pharyngitis.—Sometimes present from the onset. The appearance of the fauces varied from a mild congestion to a generalised œdema with gelatinous exudate. No special organisms were found on direct smear or culture.

Chest signs.—Cough was always present, and in 68% of cases it was accompanied by physical signs in the chest. These varied from a mild bronchitis to lobar consolidation, commonly a patchy basal consolidation.

Mental changes.—All cases showed some degree of mental change ranging from slight intellectual blunting to either coma or mania. Amnesia for the whole febrile period was not uncommon.

Flushing and cyanosis.—This was seen in all Europeans and was usually apparent by the fourth day and sometimes earlier. It does not appear to be related to the degree of pulmonary involvement, or to the cardiac efficiency, as shown by the pulse rate and blood pressure. By the third week, when there are raised pulse rate and signs of cardiac inefficiency, the cyanosis has usually disappeared.

Headache.—A prominent and early symptom in all cases. Its severity, localisation to the frontal and retro-orbital regions and accompanying photophobia are of value in early diagnosis.

Secondary Fever.—This interesting late rise in fever following a short remission, was described by Nagayo (1923) but has not been recorded in Malaya or India. The second febrile period lasts 3–5 days and is not accompanied by any recrudescence of symptoms.

Mortality and prognosis—The favourable death-rate of 6% in 1000 cases is, in part, due to the early occurrence of deaths in forward medical units and before evacuation to hospital level The relative case-mortality was 7½% in Europeans and 5% in Indians In military practice age is of little significance, 28 years being the average age both of fatal cases and survivors. Deaths in the first few weeks were due to cerebral toxæmia, and in the later weeks to septic complications Gross mental changes, particularly mania, or a rising pulse-rate with a falling temperature, are of grave significance

Diagnosis—In most cases an accurate clinical diagnosis is possible by the third or fourth day Even in the absence of a rash the apathetic, flushed, cyanosed patient with frontal headache and tender enlarged lymph-glands is characteristic

The Weil-Felix reaction is of value in atypical cases and to confirm the clinical diagnosis Significant agglutination is only obtained to the XK proteus strain, and using Dreyer's technique 1/200 can be taken as the diagnostic titre Fig 2 shows the results of 800 agglutinations (XK) from 500 cases, in each of which at some stage of the disease a titre of over 1/200 was obtained In the figure 1/200 is taken as the arbitrary diagnostic titre The percentage of cases showing titres above or below this figure is shown for each day from the third to the thirtieth The figure demonstrates that negative readings may be obtained on any day of the disease, but that between the eleventh and thirteenth days 80% of the readings are over 1/200

A misleading agglutination reaction was seen in 6 cases in which an early anamnestic rise to TO (up to 1/640) occurred with a negative XK reading, this was followed in the third and fourth weeks by a falling TO and a rising XK, the latter often to very high titre This rise occurring during the defervescence of the fever is thought to be concurrent with the development of immunity

TABLE II—WHITE CELL COUNTS IN 500 CASES

Week	Total white cells per c mm	Differential counts %			
		Polymorphs	Lymphocytes	Monocytes	Eosinophils
1	6500	56	36	6	1
2	5800	50	43	5	2
3	7800	50	42	5	3
4	7200	53	39	4	4
5	8000	52	37	5	6
6	9200	52	39	4	5

The leucocyte-counts in 500 cases are analysed in table II. Apart from complications, the count is substantially normal throughout, and of no positive assistance in diagnosis

Complications and intercurrent disease (analysis of 1000 cases)—Malaria, amœbic dysentery, infective hepatitis, and pulmonary tuberculosis were the common forms of intercurrent infection and required appropriate treatment Lobar pneumonia, pleural effusion, lung abscess, and empyema occurred as complications in the third or later weeks in 10%

Hæmorrhagic phenomena were noted in 9%, and included subconjunctival hæmorrhage, epistaxis, hæmoptysis, hæmatemesis, hæmaturia, and rectal hæmorrhage Venous thrombosis occurred in 2 cases Two cases of symmetrical gangrene were seen, one died and the other, with incipient gangrene of both hands, made a complete recovery after bilateral cervical sympathectomy

Excluding nerve deafness (see above) nervous sequelæ occurred in 2% These included 7 cases of retrobulbar neuritis, and 12 cases of a fleeting but painful paralysis of various muscle groups in the shoulder girdle

Convalescence—Muscular pains, particularly in the legs are usual in the early stages Tachycardia is also common but in most cases is not persistent A follow-up of these cases has not been possible, but from questioning men who returned to duty it appears that some have been placed temporarily in a lower medical category with a diagnosis of effort syndrome

Undue attention by the medical officer to the patient's cardiac state is often a determining factor in the development of this cardiac neurosis. Long convalescence is always necessary and several months may pass before the patient is again fit for active military duties

TREATMENT

These patients do not travel well after the fifth day of fever, and should in no circumstances be moved between the seventh and twentieth days The alternatives are, therefore, either to nurse the cases in forward units, or to make an early clinical diagnosis and evacuate to hospital by air

Treatment is symptomatic, and skilled nursing is of vital importance The diet should be of high calorie value, easily assimilable, and an adequate intake of fluid and salt should be ensured

Lumbar puncture is useful in the relief of headache and of cerebral symptoms The cerebrospinal fluid shows no constant changes in pressure or constituents Paraldehyde, or morphine and hyoscine, may safely be administered to quieten the restless and sleepless patient Mepacrine should always be given to suppress intercurrent malaria The sulphonamides and penicillin are valuable in the treatment of secondary infective complications such as lobar pneumonia The white-cell count is a useful guide in this connexion, and in the absence of a leucocytosis these drugs should be withheld, for they are ineffective against simple rickettsial pneumonia

Convalescent serum was tried in a few cases but only in small doses No clinical improvement was observed.

SUMMARY

From a study of the epidemiological, clinical, and pathological features of a group of cases of XK typhus on the India-Burma border it is apparent that they do not differ in any significant respect from the "tsutsugamushi" fevers of Japan and Malaya

The clinical findings in 500 cases are analysed, and the mortality, complications, and treatment of 1000 cases are described

Attention is drawn to the importance of an early clinical diagnosis and its bearing on evacuation policy

The value of the agglutination of *Proteus XK* suspensions is discussed

My thanks are due to Brigadier I G W Hill for his help in preparing this paper and to Lieut -Colonel M H P Sayers for his enthusiastic assistance during the epidemic; also to the many medical officers who helped to maintain a standard system of records.

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PENICILLIN IN EXPERIMENTAL PSITTACOSIS OF MICE

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VIRUS infections, with few exceptions, have proved unresponsive to treatment with the new chemotherapeutic agents In the case of the sulphonamides this is hardly surprising, for whether viruses are unorganised autocatalytic products of deranged cells or micro-organisms so committed to a parasitic mode of life as to have lost most, if not all, independent metabolic activity, one would not expect chemotherapeutic agents which act by interfering with the enzyme systems of the infected micro-organism to be effective And those exceptional viruses which have proved susceptible to sulphonamides—the viruses of trachoma, inclusion conjunctivitis, lymphogranuloma inguinale, and the virus of mouse pneumonia described by Nigg (1942)—all belong to that group of large viruses which are distinguished from the rest not only by their size and the fact that they stain readily by Castañeda's method, but also by their great morphological resemblance to bacteria. If viruses are

TABLE I (EXPT 1)

Penicillin treatment 500 units in water subcutaneously at 10 AM and 2 PM; 1000 units in sesame oil at 5 PM Continued for 8 days, each mouse receiving a total of 15 500 units Commenced immediately after infection

Treatment of mice	Infection with psittacosis virus Suspension of mouse spleen in saline following dilutions I p injection of 0 3 c.cm. of 0 3 c.cm virulent mouse-spleen suspension diluted 10^{-4} I p (produced fatal result in 2 control mice)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
Nil	D5 +	D6 +	D6 +	D7 +	D8 +	D9 +	D9 +	D9 +	D8 +	D25 +	D18 +	
Penicillin	S	S	S	D25 −	S	D−5(+)	S	D11 +	S	S	S	S
Test of immunity of survivors on 31st day	S	S	S	S	S	S	S	S	S	S	S	S

D = died day of death indicated by numeral S = survived + = virus seen in spleen smear (+) = No virus seen in spleen
D = died day of death indicated by numeral S = survived + = virus seen in spleen smear (+) = No virus seen in spleen
but demonstrated by passage — = No virus found in spleen s c. = subcutaneous I p = intraperitoneal
Similar symbols used in subsequent tables

highly specialised parasitic micro-organisms it is pre
closely these large ones which one might expect to be less
fully adapted to this mode of existence and therefore
susceptible to attack by sulphonamides

The mode of action of penicillin is not understood but
It is clear that it is bacteriolytic as well as being bacterio-
static (Todd 1945), so one might possibly expect it to be
more effective against viruses than the sulphonamides
have proved to be Little work on this subject has been
done as yet, and here again the recorded successes have
been against infections with the large Castañeda positive
viruses Hellman and Herrell (1944) have produced
evidence that experimental psittacosis in the mouse
responds to treatment with penicillin It is true that the
amount of penicillin they found necessary was very
large—1000 units per mouse divided between five doses
in the 24 hours, repeated for 8 days—but the results
obtained in their two published experiments were
unequivocal, particularly in the second experiment where
22 treated mice all survived for 30 days without showing
any signs of illness whereas a similar number of control
mice were all dead in 6 days It is interesting to note
that the survivors were none the less infected, as was
shown by successful passage with suspensions of liver
and spleen from 11 of 12 of the mice killed and examined
at the end of the experiment

Parker and Diefendorf (1944) have tested the effect of
penicillin on the multiplication of viruses in a Rivers Li
medium and in incubated hens eggs In the former
type of experiment the chick embryo minces in tyrode
contained 10 units of penicillin per c cm of medium
and virus multiplication was compared with that
obtained in a similar medium devoid of penicillin In the
second type of experiment 500 units of penicillin were
injected into each egg either at the time of infection of
the chorio-allantoic membrane or 24 hours before, and
with those in control eggs The viruses examined in this
way were equine encephalomyelitis vaccinia, psitta
cosis meningopneumonitis—which is probably psittacosis
virus of pigeon origin (Beck Eaton, and O'Donnell 1944)
—and St Louis encephalitis; negative results were
obtained with all except the viruses of meningopneu-
monitis, and psittacosis and with the latter the results
were not nearly so impressive as those obtained by
Hellman and Herrell (1944)

Recently Sorsby (1945) has shown that inclusion
conjunctivitis in the infant responds rapidly and satis-
factorily to local treatment with penicillin There is
therefore no doubt as to the sensitivity of some of these
large viruses to penicillin, though in the case of psittacosis
virus it is not clear how sensitive the virus really is and
whether this sensitivity is of such an order as to make this
form of therapy worthy of trial in human infections
which are often serious and for which no specific treat-
ment is available It was with this object in view that
the following experiments were made

EXPERIMENTAL DATA

Strain of virus—The strain used throughout—MOII 154—was isolated from a parrot in 1940 and had been maintained in mice since then by frequent passage Spleens of mice killed when moribund on the third day after infection by the intraperitoneal route were suspended in saline to give a 2 5% suspension From such a stock suspension, clarified either by short centrifugation or sedimentation in the refrigerator further dilutions were made with saline immediately before infection

Mice—Adult white mice weighing 18–20 g supplied by the same dealer, were used throughout

Penicillin—Sodium penicillin (Pfizer) was dissolved in water in sesame oil or in 20% g latin

Expt 1—Falling decimal dilutions, 10^{-1} to 10^{-6} were injected intraperitoneally into mice in a dose of 0 3 c cm; 4 mice were employed for each dilution Penicillin treatment was given to 2 mice in each dilution group the other 2 acting as controls Treatment was begun immediately after infection and consisted of 500 units in water at 10 AM and again at 2 PM, and 1000 units in sesame oil at 5 PM The penicillin was given subcutaneously and treatment was continued for 8 days making a total of 15 500 units per mouse The mice were observed for 31 days and spleens of those dying were examined for the presence of psittacosis virus by impression preparations stained by Castañeda and if necessary by mouse passage At the end of the period of observation the survivors were tested for immunity by reinoculation with a certainly lethal dose of psittacosis virus resistance to this test was taken as evidence of persistent infection

The results of this experiment are given in table I from which it will be seen that whereas all the 10 control mice died, 6 of the treated survived Of the 4 mice that died virus could be demonstrated in the spleen either by direct microscopical examination or by mouse passage but since the 6 survivors all resisted reinoculation with a dose of psittacosis virus which killed 2 control mice in 6 day and were therefore almost certainly suffering from a persisting though silent infection the demonstration of

TABLE II (EXPT 2)

Penicillin treatment: Same as in expt 1 except that 1(00) units at 7 PM given in water

Treatment of mice	Infection with psittacosis virus Suspension of mouse spleen in saline following dilutions I p injection of 0 2 c cm of 0 2 c cm virulent mouse-spleen suspension diluted 10^{-4} I p (produced fatal result in 4 control mice)											
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Nil	D4 +	D4 +	D5 +	D5 +	D4 +	D6 +	D6 +	D4 +	D4 −	S		
Penicillin	S	S	S	S	S	S	S	S	S	S		
Test of immunity of survivors on 21st day	D5 +	D18 −	S	S	D15 −	S	S	S	S	S		

S = survived D = died day of death indicated by numeral + = virus seen in spleen smear (+) = No virus seen in spleen
s c. = subcutaneous I p = intraperitoneal

very ill When killed and examined virus could be demonstrated in all except 1 only in the spleen

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Excluding nerve deafness (see above) nervous sequelæ occurred in 2% These included 7 cases of retrobulbar neuritis, and 12 cases of a fleeting but painful paralysis of various muscle groups in the shoulder girdle

Convalescence—Muscular pains, particularly in the legs are usual in the early stages. Tachycardia is also common but in most cases is not persistent A follow-up of these cases has not been possible, but from questioning men who returned to duty it appears that some have been placed temporarily in a lower medical category with a diagnosis of effort syndrome

Undue attention by the medical officer to the patient's cardiac state is often a determining factor in the development of this cardiac neurosis. Long convalescence is always necessary and several months may pass before the patient is again fit for active military duties

TREATMENT

These patients do not travel well after the fifth day of fever, and should in no circumstances be moved between the seventh and twentieth days The alternatives are, therefore, either to nurse the cases in forward units, or to make an early clinical diagnosis and evacuate to hospital by air

Treatment is symptomatic, and skilled nursing is of vital importance The diet should be of high calorific value, easily assimilable, and an adequate intake of fluid and salt should be ensured

Lumbar puncture is useful in the relief of headache and of cerebral symptoms The cerebrospinal fluid shows no constant changes in pressure or constituents Paraldehyde, or morphine and hyoscine, may safely be administered to quieten the restless and sleepless patient Mepacrine should always be given to suppress intercurrent malaria The sulphonamides and penicillin are valuable in the treatment of secondary infective complications such as lobar pneumonia The white-cell count is a useful guide in this connexion, and in the absence of a leucocytosis these drugs should be withheld, for they are ineffective against simple rickettsial pneumonia.

Convalescent serum was tried in a few cases but only in small doses No clinical improvement was observed.

SUMMARY

From a study of the epidemiological, clinical, and pathological features of a group of cases of XK typhus on the India-Burma border it is apparent that they do not differ in any significant respect from the "tsutsugamushi" fevers of Japan and Malaya

The clinical findings in 500 cases are analysed, and the mortality, complications, and treatment of 1000 cases are described

Attention is drawn to the importance of an early clinical diagnosis and its bearing on evacuation policy

The value of the agglutination of *Proteus XK* suspensions is discussed

My thanks are due to Brigadier I G W Hill for his help in preparing this paper and to Lieut -Colonel M H P Sayers for his enthusiastic assistance during the epidemic; also to the many medical officers who helped to maintain a standard system of records

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PENICILLIN IN EXPERIMENTAL PSITTACOSIS OF MICE

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Virus infections, with few exceptions, have proved unresponsive to treatment with the new chemotherapeutic agents In the case of the sulphonamides this is hardly surprising, for whether viruses are unorganised autocatalytic products of deranged cells or micro-organisms so committed to a parasitic mode of life as to have lost most, if not all, independent metabolic activity, one would not expect chemotherapeutic agents which act by interfering with the enzyme systems of the infective micro-organism to be effective And those exceptional viruses which have proved susceptible to sulphonamides—the viruses of trachoma, inclusion conjunctivitis, lymphogranuloma inguinale, and the virus of mouse pneumonia described by Nigg (1942)—all belong to that group of large viruses which are distinguished from the rest not only by their size and the fact that they stain readily by Castañeda's method, but also by their greater morphological resemblance to bacteria If viruses are

TABLE I (EXPT 1)

Penicillin treatment: 500 units in water subcutaneously at 10 AM and 2 PM 1000 units in sesame oil at 5 PM. Continued for 8 days, each mouse receiving a total of 15,500 units Commenced immediately after infection

Treatment of mice	Infection with psittacosis virus Suspension of mouse spleen in saline. I p injection of 0 3 c cm of following dilutions					
	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	
Nil	D5 + D6 +	D6 +, D7 +	D8 + D9 +	D9 + D9 +	D8 + ; D*5 +	
Penicillin	S S	S ; D25 −	S D*5(+)	S ; D11 +	S D18 +	
Test of immunity of survivors on 31st day	0 3 c.cm virulent mouse-spleen suspension diluted 10^{-1} i p (produced fatal result in 2 control mice)					
	S S	S	S	S	S	

D = died, day of death indicated by numeral. S = survived + = virus seen in spleen smear (+) = No virus seen in spleen smear but demonstrated by passage — = No virus found in spleen s c = subcutaneous. i.p. = intraperitoneal
Similar symbols used in subsequent tables

highly specialised parasitic micro-organisms it is precisely these large ones which one might expect to be less fully adapted to this mode of existence and therefore susceptible to attack by sulphonamides

The mode of action of penicillin is not understood but it is clear that it is bacteriolytic as well as being bacteriostatic (Todd 1945), so one might possibly expect it to be more effective against viruses than the sulphonamides have proved to be Little work on this subject has been done as yet, and here again the recorded successes have been against infections with the large Castañeda positive viruses Hellman and Herrell (1944) have produced evidence that experimental psittacosis in the mouse responds to treatment with penicillin It is true that the amount of penicillin they found necessary was very large—1000 units per mouse divided between five doses in the 24 hours, repeated for 8 days—but the results obtained in their two published experiments were unequivocal, particularly in the second experiment where 22 treated mice all survived for 30 days without showing any signs of illness, whereas a similar number of control mice were all dead in 6 days It is interesting to note that the survivors were none the less infected, as was shown by successful passage with suspensions of liver and spleen from 11 of 12 of the mice killed and examined at the end of the experiment.

Parker and Diefendorf (1944) have tested the effect of penicillin on the multiplication of viruses in a Rivers Li medium and in incubated hens' eggs. In the former type of experiment the chick embryo mince in tyrode contained 10 units of penicillin per c cm of medium and virus multiplication was compared with that obtained in a similar medium devoid of penicillin In the second type of experiment 500 units of penicillin were injected into each egg either at the time of infection of the chorio-allantoic membrane or 24 hours before, and the size and number of lesions developing were compared with those in control eggs The viruses examined in this way were equine encephalomyelitis, vaccinia, psittacosis, meningopneumonitis—which is probably psittacosis virus of pigeon origin (Beck, Eaton, and O'Donnell 1944)—and St Louis encephalitis; negative results were obtained with all except the viruses of meningopneumonitis, and psittacosis, and with the latter the results were not nearly so impressive as those obtained by Hellman and Herrell (1944)

Recently Sorsby (1945) has shown that inclusion conjunctivitis in the infant responds rapidly and satisfactorily to local treatment with penicillin There is therefore no doubt as to the sensitivity of some of these large viruses to penicillin, though in the case of psittacosis virus it is not clear how sensitive the virus really is and whether this sensitivity is of such an order as to make this form of therapy worthy of trial in human infections which are often serious and for which no specific treatment is available It was with this object in view that the following experiments were made

EXPERIMENTAL DATA

Strain of virus.—The strain used throughout—MOH 154 7—was isolated from a parrot in 1940 and had been maintained in mice since then by frequent passage Spleens of mice killed when moribund on the third day after infection by the intraperitoneal route were suspended in saline to give a 2 5% suspension From such a stock suspension, clarified either by short centrifugation or sedimentation in the refrigerator further dilutions were made with saline immediately before infection

Mice.—Adult white mice weighing 18–20 g, supplied by the same dealer, were used throughout

Penicillin.—Sodium penicillin (Pfizer) was dissolved in water in sesame oil, or in 20% gelatin

Expt. 1.—Falling decimal dilutions, 10^{-1} to 10^{-4}, were injected intraperitoneally into mice, in a dose of 0 3 c cm, 4 mice were employed for each dilution Penicillin treatment was given to 2 mice in each dilution group, the other 2 acting as controls. Treatment was begun immediately after infection and consisted of 500 units in water at 10 AM and again at 2 PM and 1000 units in sesame oil at 5 PM. The penicillin was given subcutaneously and treatment was continued for 8 days, making a total of 15 500 units per mouse The mice were observed for 31 days and spleens of those dying were examined for the presence of psittacosis virus by impression preparations stained by Castañeda and if necessary by mouse passage At the end of the period of observation the survivors were tested for immunity by reinoculation with a certainly lethal dose of psittacosis virus, resistance to this test was taken as evidence of persistent infection

The results of this experiment are given in table I from which it will be seen that whereas all the 10 control mice died 6 of the treated survived Of the 4 mice that died virus could be demonstrated in the spleen either by direct microscopical examination or by mouse passage, but since the 6 survivors all resisted reinoculation with a dose of psittacosis virus which killed 2 control mice in 6 days, and were therefore almost certainly suffering from a persisting though silent infection, the demonstration of

TABLE II (EXPT 2)

Penicillin treatment: Same as in expt 1 except that 1000 units at 5 PM given in water

Treatment of mice	Infection with psittacosis virus: Suspension of mouse spleen in saline I p injection of 0 3 c.cm of following dilutions				
	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}
Nil	D4 + ; D4 +	D5 + D3 +	D6 + D6 +	D6 + D7 +	D4 − D*
Penicillin	D5 + D5 +	S S	S S	S ; S	S S
Test of immunity of survivors on 31st day	0 3 c cm virulent mouse-spleen suspension diluted 10^{-1} i p (produced fatal result in 4 control mice)				
		D5 + D18 −	S ; S	D15 − S	S S

* Recovered after appearing very ill When killed and examined virus could be demonstrated microscopically in the spleen

TABLE III (EXPT 3)

Penicillin treatment · 500 units in water subcutaneously at 10 AM and 2 PM, 1000 units in water at 5 PM. Commenced immediately after infection

Infection with psittacosis virus · Suspension of mouse spleen in saline I p injection of 0 3 c cm. diluted 10 ⁴ Penicillin treatment continued for.			
2 days (Total, 1000 units)	4 days (Total, 8000 units)	6 days (Total, 12,000 units)	No penicillin
D6 + D9 + D9 + S	S S S S	S S S S	D7 + D7 + D7 + D9 +
Test of immunity of survivors on 50th day 0 3 c cm virulent mouse spleen diluted 10 ⁴ I p (produced fatal result in 4 control mice)			
S	S S S S	S S S S	

TABLE IV (EXPT. 4)

Penicillin dissolved in 20% gelatin to give 2000 units per c cm Subcutaneous injection of 0 4 c cm at 24-hour intervals for 4 days First injection immediately after infection

Infection with psittacosis virus Suspension of mouse spleen in saline I p injection of 0 3 c cm of a dilution of 10 ⁴	
8 mice given penicillin and observed for a month	4 controls
S S S S S S S S	D7+ D7+ D8+ D9+

virus in the spleens of those penicillin-treated animals which died is no proof that their death was due to psittacosis There was, in fact, some evidence to suggest the contrary, because the 4 deaths had occurred irregularly and bore no relation to the infecting dose of virus The possibility that the deaths had been due to the activation of pre-existing salmonella infection was considered, but no salmonella were isolated from the spleen of these mice The impression was gained that the sesame oil in which the penicillin given at 5 PM was suspended was not without toxicity. It was not absorbed and collected under the skin of the back where it had been injected, in some instances tracking under the skin for considerable distances In view of this the sesame oil was abandoned in the subsequent experiments and the greater size of the evening dose was alone relied on to maintain an adequate level of penicillin in the tissues through the night

Expt. 2 was a replica of the first experiment except that the 1000 units of penicillin injected at 5 PM was dissolved in water. The findings are given in table II. Unfortunately of the 2 control mice receiving the smallest dose of virus, one died on the fourth day from some intercurrent though undetermined infection, while the other survived obvious infection with psittacosis Despite this and the fact that the 2 treated mice which had received the largest infecting dose succumbed, it is obvious, as in the first experiment, that the administration of penicillin had had a definite and beneficial effect. In this experiment only 5 out of the 8 survivors resisted reinoculation with a dose of virus which killed 4 control mice in 7–9 days, though virus could be found in the spleen of only 1 of the 3 that succumbed to the test

Expt 3, the results of which are recorded in table III, was designed to find out if the total amount of penicillin used per mouse in the previous experiments was necessary to prevent a fatal infection Infection was made with a fixed dose of virus, and the 16 mice so inoculated were divided into four groups One group remained untreated. The remaining three groups were given the same daily course of penicillin injections as in experiment 2 but treatment was continued for varying periods—2 days in one group, 4 days in another, and 6 days in the third It is obvious that this dosage of penicillin given for 4 days prevents the development of a fatal infection just as surely as when the treatment is continued for 6 days, whereas 2 days' treatment is insufficient The surviving mice again proved resistant to reinfection

Expt 4 —Some preliminary trials in mice having shown that incorporation of the penicillin in 20% gelatin delayed absorption, and that even 24 hours after the subcutaneous injection of 800 units in this medium the serum of a mouse was still inhibitory to the Oxford strain of *Staphylococcus pyogenes*, penicillin treatment in this experiment was given in the form of a daily injection of 800 units in 20% gelatin repeated four times Twelve mice were infected by the intraperitoneal injection of 0 3 c cm. of a virulent mouse-spleen suspension diluted 10⁴, and 8 mice were treated, the remaining 4 acting as controls. As will be seen from table IV, all the controls died while the treated mice survived for a month, having shown no signs of illness. The survivors were not treated for immunity because it was thought that sufficient evidence on this point had already been obtained

Expt 5 —In the previous experiment four daily injections of 800 units of penicillin, the first given immediately after infection, clearly protected the mice against a lethal dose of psittacosis virus This last experiment was made to find out whether a smaller dose of penicillin given in this way would be effective, as will be seen from the results given in table V, a smaller dose is insufficient

COMMENT

These experiments clearly show that psittacosis virus is susceptible to penicillin when in the tissues of the mouse and amply confirm the findings of Heilman and Herrell. The amount of penicillin required to keep in check infection with this virus to the extent of making the infection subclinical is, however, very great, and, if one was entitled to argue, from mouse to man would represent something in the region of 11 mega-units for the effective treatment of a human case It is true that a smaller total dose would quite possibly have been effective had the injections of penicillin been given at shorter intervals so as to maintain the blood concentration at a more even level, and that in man a smaller quantity might well prove effective when administered by continuous intramuscular infusion or intravenous drip. In any case it would be worthy of trial since human infections with psittacosis virus are often serious and no satisfactory specific treatment is available. The only reported instance of a human case of psittacosis treated with penicillin that we have been able to find is that of Turgassen (1944) where 100,000 units a day for 8 days commencing on the fifth day of illness did not give a dramatic response although the temperature was normal by the tenth day of illness and the patient made a good recovery.

There are a number of other aspects of this question which it would be of great interest to investigate—the mode of action of penicillin on this virus, whether it can destroy the virus in a state of quiescence outside the body, and whether in the body it is only the virus outside the cells which is susceptible, these we intend to go into when time permits The fact that mice which survived psittacosis infection as the result of penicillin treatment were commonly found to be immune to reinfection and therefore none the less infected, suggests that, just as in the case of specific antibody, virus inside cells is protected against the action of penicillin This also suggests that psittacosis virus which is not actually multiplying may be susceptible since it is only in the intracellular environment that the virus is thought to multiply.

TABLE V (EXPT 5)

Penicillin given s c in 20% gelatin, four doses at 24-hour intervals, the daily dose varying from 100 to 800 units Observed for a month Treatment begun immediately after infection

Infection with psittacosis virus Suspension of virulent mouse spleen in saline I p injection of 0 3 c cm of a 10⁻⁴ dilution			
Mice given 800 units pen daily	Mice given 400 units pen daily	Mice given 100 units pen daily	Mice untreated
D8 + S S S S S	D9 + D9 + D11 + D11 + S S	D8 + D10 + D14 S S S	D8 + D8 + D8 + D8 + D10 + D10 +

Pen = penicillin

References at foot of opposite page

ASPIRATION LIVER BIOPSY

TECHNIQUE AND DIAGNOSTIC APPLICATION

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DESPITE the battery of laboratory tests available for studying hepatic diseases, diagnosis is often difficult. Any safe, sure diagnostic method is therefore to be welcomed. When Iversen and Roholm (1939) published their series of 100 aspiration liver biopsies with no mishaps, it was believed that this method might become generally applicable. However, early results obtained by Dible, McMichael, and Sherlock (1943) indicated that *the method was not without risk. Later modifications* in the selection of cases and in technique have increased the safety of the procedure, and we now believe that aspiration liver biopsy has a definite place in the elucidation of obscure hepatic diseases. Therefore we publish *the technique in detail with some indications of its use in* diagnosis.

Technique of Aspiration Liver Biopsy

PREPARATION OF PATIENT

To a jaundiced patient it is advisable to give a vitamin-K preparation for three days before the puncture. If the jaundice is non-obstructive (urobilin present in the urine), two 5 mg. tablets of "Kapilon" are given by mouth three times a day. If the jaundice is obstructive, the vitamin must be administered intramuscularly; 5 mg. daily is a suitable dose.

In every case, before biopsy is performed, the patient's blood-group should be known, and two pints of compatible blood should be readily available. Aspiration liver biopsy should not be performed unless adequate facilities for blood transfusion are available in case of complicating haemorrhage. A sedative is unnecessary before puncture.

HEPATIC PUNCTURE

The patient lies supine in bed with the right side as near the edge of the bed as possible. A firm pillow may be placed under the left side in the hollow of the bed, so that the body is slightly tilted to the right. The right arm is placed behind the head. A site is chosen in the ninth or tenth intercostal space in the middle or anterior axillary line. After cleansing, the skin is anæsthetised with 2% procaine solution. A long fine-bore needle is used to infiltrate the pleura and is then passed through the diaphragm to anæsthetise the peritoneum and the capsule of the liver. At least 10 ml. of local anæsthetic is needed. If the skin is tough, a preliminary nick may then be made with a scalpel. The cannula used is 15 cm. long and 1 mm. in bore. It is fitted with a handled trocar. The instrument is passed through the skin, and the patient is then instructed to "take a deep breath in, let it out, and then hold your breath." This displaces the lung upwards and ensures apposition of diaphragmatic and costal pleura. The trocar and cannula are now pushed through the diaphragm into the right lobe of the liver. The trocar is not withdrawn until the instrument is fully half an inch inside the liver substance. The cylinder of liver tissue is then punched out by pushing the cannula on a further 4–5 cm. A 20 ml. "Record" syringe is connected to the cannula, and suction is applied and maintained while the cannula is withdrawn. The puncture wound in the skin is sealed with collodion. The fragment of liver is usually found in the barrel of the syringe; occasionally it remains in the cannula. The aspiration of blood with the biopsy specimen need not occasion alarm.

AFTERCARE

As a little local pain may follow puncture, morphine gr. ¼ or gr. ½ is given subcutaneously, according to the size and type of patient. This allays discomfort and prevents restlessness. If necessary, a further sedative, such as barbitone soluble gr. 10, may be given in the evening. The pulse is charted hourly for the first 24 hours after biopsy; the physician should be called if the pulse-rate shows a rise. Routine visits should be paid 4 and 8 hours after biopsy. A very careful watch must be kept on the patient, and if there is any sign of haemorrhage the cross matched blood should be administered. Absolute rest in bed is essential for 24 hours. The patient can then be up and about and if desired can leave hospital 48 hours after the liver puncture.

The procedure is attended with very little disturbance to the patient. During the puncture there may be a complaint of a drawing feeling across the epigastrium. Afterwards some patients have a slight ache in the right side for about 24 hours, and some complain of pain referred from the diaphragm to the right shoulder. Most patients agree that the discomfort compares favourably with that associated with sternal or lumbar puncture. Thirty patients had more than one biopsy, one had four.

DIFFICULTIES

There may be failure to get an adequate sample of liver. Hoffbauer (quoted by Watson 1944) had 40% failures with the Tripoli and Fader (1941) technique. Iversen and Roholm (1939) reported a 10–15% failure rate; van Beek and Haex (1943), however, using the same method, state that the puncture failed but rarely. In our first 120 biopsies there were 10% of failures; in the next 138 only 2%. Difficulties arise most often in hepatic cirrhosis, especially if there is associated ascites. In cirrhosis the tough liver is difficult to pierce and a few liver-cells may be extracted leaving the fibrous framework behind. In ascites the liver is very "*ballottable*" and is difficult to transfix. A paracentesis abdominis should be undertaken before the liver biopsy is attempted, and the patient should lie well over on the right side during the puncture. This brings the liver into contact with the chest wall. Another source of difficulty may be pulmonary emphysema; the liver is pushed downwards by the low diaphragm. It is very easy for the trocar to pass above the liver. If a low diaphragm is suspected before biopsy, the chest should be radiographed, and if necessary the puncture can be made through a lower intercostal space.

TABLE I—MORTALITY OF ASPIRATION LIVER BIOPSY

Author	Date	Liver biopsies	Deaths
Bingel	1923	100	2
Olivet	1926	140	3
Huard May Joyeux	1935	163	0
Baron	1938	40	1
Iversen Roholm	1939	100	0
Tripoli Fader	1941	14	0
Hatieganu Sprecher Radu Macavei	1943	45	0
Van Beek Haex	1943	200	0
Hoffbauer	1943	65	0
Present series	1945	264	2
Total		1700	8

RISKS

The fatality rates in published cases are shown in table I, the combined rate being 0·47%. In the first 126 punctures in this series (Dible et al. 1943) there were two deaths, one of them in a patient already moribund with subacute necrosis of the liver. Since then a further 138 punctures have been performed with no evidence of haemorrhage. This lessening of risk may be attributed to changes in technique and to more careful selection of cases.

The trocar used in the original series of 126 punctures was 2 mm. in diameter and 10 cm. long; the new instrument is longer and narrower. In one of the fatal cases the blood had leaked from a cylindrical hole on the liver surface. The narrower cannula makes a smaller wound in the liver; the longer instrument allows the sharp trocar

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to be pushed well into the liver before it is withdrawn, the incision in the capsule is then clean-cut and can heal easily, while the small cylinder of liver is taken deeply in the liver substance

Accidents will be prevented if the biopsy is confined to patients who are coöperative It is dangerous if the patient breathes with the trocar in the liver, as a longitudinal rent can then be produced For this reason speed in puncture is essential Any modification in technique, such as the injection of an anticoagulant through the trocar or the intercostal use of a more complicated needle, such as that of Tripoli and Fader, will add to the time taken for the biopsy and hence increase the risk of tearing the liver The risk of hæmorrhage is greatest in the severely jaundiced, especially if the jaundice is due to acute parenchymatous liver disease We have never met clinical evidence of hæmorrhage in the non-jaundiced group Table II shows a comparison of the results in the previous series with those of the new technique in jaundiced patients

TABLE II—INCIDENCE OF HÆMORRHAGE AFTER ASPIRATION LIVER BIOPSY IN JAUNDICED SUBJECTS

	Previous series (1943), short 2 mm bore cannula	Present technique long 1 mm. bore cannula
Bleeding	5	0
No bleeding	78	74

INSPECTION AND FIXATION OF BIOPSY SPECIMEN

Some information may be gained by inspection of the biopsy specimen Fatty livers have a characteristic greasy look. Biopsy specimens of livers with excess fibrous tissue tend to crumble into fragments with a lobulated contour If a malignant deposit has been punctured, the dull white appearance of the biopsy specimen is characteristic

The most useful routine fixative is absolute alcohol Though it dissolves out red cells, it preserves the glycogen in the liver-cells and enables Best's carmine stain to be applied To demonstrate the elements of blood in the hepatic sinusoids, formol-saline is the more satisfactory fixative. Fat can be shown by fixing the material in Bouin's solution followed by 2% osmic acid. After fixation the specimen is embedded, sectioned longitudinally along the line of the cylinder, and stained in the usual way If desired, the sample can be examined bacteriologically.

Reliability of Biopsy Specimens in Assessing Liver Histology

The use of these small biopsy specimens as representative of the pathology of the whole organ may be questioned Pathologists, including Stewart (1917), Miller and Rutherford (1923), Bergstrand (1930), and Lucké (1944), recorded that in massive hepatic necrosis in man the left lobe of the liver was more damaged than the right Himsworth and Glynn (1944) mentioned similar findings in experimental "trophopathic hepatitis" In our cases of acute hepatitis the histological damage in the biopsy specimens corresponded well with the clinical severity of the disease, and there was little variation from lobule to lobule. Excluding the obviously localised conditions—e g, malignant metastases, abscesses, and cysts—most other examples of human liver disease have a reasonably uniform histology Thirty cases came eventually to necropsy, in each the histology of the biopsy specimen was a fair sample of the liver as a whole It must be emphasised that the preparation obtained from these biopsies is not a smear of liver-cells but a section of liver tissue comprising about 10–20 lobules

Use of Biopsy Specimens in Diagnosis

The distribution of the case material is shown in table III The diagnostic potentialities of the method will be illustrated by examples from some of the groups

ACUTE HEPATITIS

Aspiration biopsy in the study of this condition has been discussed elsewhere (Dible et al 1943) If the biopsy is performed early in the jaundiced phase, the acute liver inflammation presents a characteristic picture, and a diagnosis can readily be made from other common causes of jaundice If the biopsy is postponed until convalescence, normal liver tissue may be observed, and diagnosis is then impossible

CIRRHOSIS OF THE LIVER

It is in this group that clinical diagnosis, even with biochemical assistance, may be very difficult Liver biopsy often supplies a definite answer This is illustrated by the following case

CASE 1 —A soldier, aged 35, had arsenotherapy jaundice in February, 1944 This never fully cleared up, and in July, 1944, there was a severe exacerbation of jaundice Recovery was slow, and in January, 1945, the patient was invalided from the Army, and in March, 1945, admitted to Hammersmith Hospital There was no other history of jaundice, and the patient had never served overseas The present complaints were some dyspnœa on exertion and discomfort in the left side of the abdomen There was no jaundice, the liver edge was felt 4 cm below the costal margin and was firm and slightly tender The spleen was palpable half-way to the umbilicus There was no ascites or evidence of portal vein obstruction The urine contained an excess of urobilin but was not otherwise abnormal. Laboratory tests were mostly negative, plasma bilirubin, phosphatase, cholesterol, and differential plasma proteins, the colloidal-gold test (Maclagan 1944), the intravenous hippuric-acid test (Quick, Ottenstein, and Weltchek 1938), and intravenous galactose test (King and Aitken 1940) were all normal There was 20% retention of bromsulphthalein 30 min after the injection of 5 mg per kg of body-weight (technique of Helm and Machella 1942).

TABLE III—CASES STUDIED BY ASPIRATION LIVER BIOPSY

Diagnosis	Cases	Biopsies
Acute hepatitis—		
Epidemic hepatitis	23	29
Arsenotherapy jaundice	54	71
Serum jaundice	10	11
Cirrhosis of the liver	21	26
Obstructive jaundice	18	27
Malignant disease of the liver without jaundice	6	8
Diseases of the blood	20	20
Kala-azar	3	3
Amyloid disease	3	3
Cardiac failure	23	25
Miscellaneous	41	41
Total	222	264

As the trocar and cannula were introduced into the liver for aspiration biopsy, the organ felt hard and granular. The histological picture was that of a fully developed portal cirrhosis There was fatty infiltration of the liver-cells (fig 1) In this case it was essential to know the exact state of the liver Laboratory tests were equivocal, aspiration liver biopsy gave a definite diagnosis

Liver biopsy is useful not only in making a diagnosis of cirrhosis but also in proving a negative We have studied cases with histories and physical signs almost identical with those of case 1, yet with a normal liver on biopsy In other cases treatment had been instituted for a hepatic cirrhosis, diagnosed by clinical or laboratory means, yet liver biopsy showed a perfectly normal liver.

OBSTRUCTIVE JAUNDICE

Aspiration liver biopsy readily distinguished obstructive icterus of short duration from other types of jaundice

CASE 2 —A man, aged 60, had had, 3 days before admission to hospital, a rigor followed by anorexia, flatulence, and a feeling of fullness in the epigastrium His stools had become pale, his urine dark Next day his sclerotics were yellow The liver was slightly tender and was enlarged 4 cm below the costal margin The gall-bladder and spleen were not palpable The urine showed bile pigments and an absence of urobilin Laboratory findings were plasma bilirubin 3 9 per 100 ml, plasma phosphatase 19 units per 100 ml, galactose tolerance was impaired, and hippuric acid synthesis was low All these findings suggested a hepatitis rather than an obstructive jaundice Liver biopsy, however, showed no accumulations of bile in the canaliculi towards the centres of the liver lobules This is a common finding in obstructive jaundice There was no hepatitis. The jaundice clear

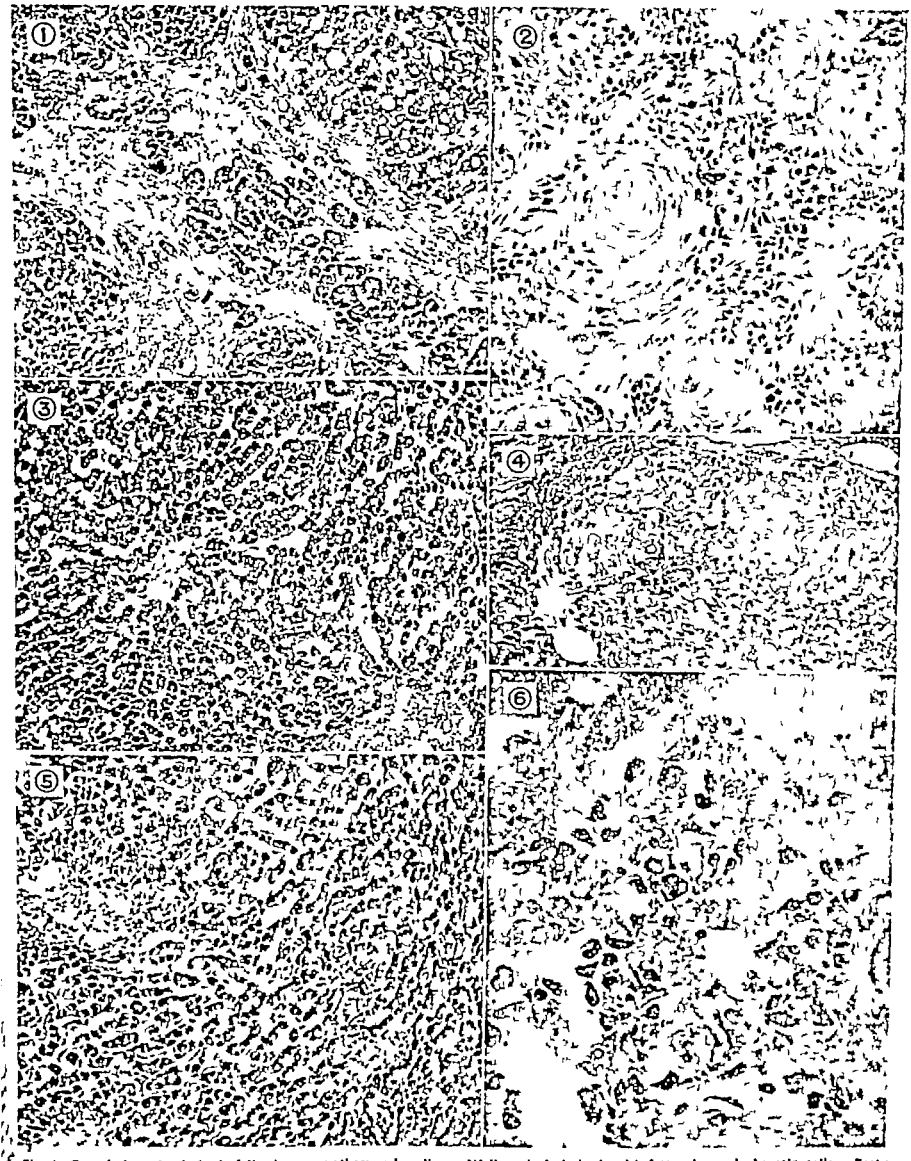

Fig 1—Case 1 hepatic cirrhosis following arsenotherapy jaundice Well-marked cirrhosis with fatty change in hepatic cells. Best's carmine stain. (× 99.)

Fig 2—Case 3 secondary hepatic squamous epithelioma with cell nests. Best's carmine stain. (× 135.)

Fig 3—Case 4 histiocytic medullary reticulosis. Increased nucleated cells in the sinusoids and portal tracts. The cells are primitive and give the impression of being formed from the sinusoidal epithelium. Best's carmine stain (× 94.)

Fig 4—Case 5 amyloid disease Heavy infiltration of hepatic sinusoids with pale-staining amyloid Modified van Gieson stain. (× 97.)

Fig 5—Case 6 kala-azar Histiocytic accumulations scattered through the liver Best's carmine stain. (× 112.)

Fig 6—Case 6 kala-azar Leishman-Donovan bodies lying within the histiocytes. Leishman's stain (× 865.)

rapidly, and cholecystograms showed a non-functioning gall-bladder The probable diagnosis was chronic cholecystitis with gall-stones

Later in the course of obstructive jaundice, diagnosis may not be so simple The secondary changes in the liver produce a picture of biliary cirrhosis which can be exceedingly difficult to differentiate from cirrhosis developing in the absence of disease of the biliary tract

MALIGNANT DISEASE OF THE LIVER WITHOUT JAUNDICE

The diagnosis of localised lesions by puncture of the liver with a narrow-bored instrument must be a matter of chance, but surprisingly often a portion of a localised lesion is obtained for section, and it may indicate the site of the primary disease.

CASE 3 —A carpenter, aged 65, complained of anorexia, epigastric discomfort, constipation, and loss of weight Apart from wasting, nothing abnormal was found on physical examination A fractional test-meal showed a histamine-fast achlorhydria Radiograms showed no abnormality in chest, œsophagus, or stomach Stools were examined on five occasions, but no occult blood was found A definite diagnosis could not be made

A fortnight later a small firm nodule was noticed in the region of the liver Liver biopsy was performed, and the specimen obtained proved on section to be a squamous celled carcinoma (fig 2) Gall-bladder, renal tract, bronchus, and œsophagus were all considered as the site of the primary lesion This latter site was finally incriminated by repeating the barium swallow, when a considerable pressure deformity and irregularity of the œsophagus were seen The diagnosis of œsophageal squamous celled carcinoma with hepatic metastases was later confirmed by autopsy

A second case in which aspiration hepatic biopsy showed squamous-celled carcinoma proved to be a symptomless bronchial carcinoma Melanocarcinoma (primary in the eye), sarcoma of the liver (primary in the uterus), and adenocarcinoma (primary in the upper rectum) have also been identified by aspiration liver biopsy This sort of positive information is of value if surgical intervention is being considered. However, if aspiration liver biopsy does not demonstrate malignant disease, its absence cannot be assumed.

DISEASES OF THE BLOOD

The use of aspiration liver biopsy in the diagnosis of obscure hematological disorders is illustrated by the following case.

CASE 4 —A grocer, aged 54, complained of exhaustion, progressive pallor, and breathlessness The skin was lemon yellow, the tongue was smooth, the spleen was just palpable, there was no hepatomegaly or lymphadenopathy, the urine constantly showed excess of urobilin, fractional test meal revealed histamine fast achlorhydria Examination of the peripheral blood showed erythrocytes 2,000,000 per c mm, Hb (Haden) 38%, colour index 1 18, mean corpuscular volume 107 5 cμ, reticulocytes 0 8%, and leucocytes 3000 per c.mm, of which 1500 were lymphocytes Smears of sternal marrow revealed a preponderance of late erythroblasts and basophil normoblasts, there were small numbers of megaloblasts

The patient was treated with iron, various liver preparations, including protolysed liver by mouth, and with ascorbic acid There was no improvement He was sustained with blood-transfusions The provisional diagnosis was megalocytic anæmia (refractory type) Six weeks later the liver was palpable and the spleen was larger Aspiration liver biopsy showed increased cells in the sinusoids and portal tracts (fig 3) The cells were primitive and gave the impression of being formed from the sinusoidal epithelium There was no evidence of phagocytic activity. There was little differentiation of the cells iron stains showed diffuse siderosis The picture most closely resembled the histiocytic medullary reticulosis described by Bodley Scott and Robb Smith (1939) The patient eventually died with terminal purpura and jaundice Necropsy confirmed the diagnosis

This case illustrates the part liver biopsy may have to play in the elucidation of "refractory" anæmias We have used the method in other blood disorders Blood formation in liver has been demonstrated in two cases of leucoerythroblastic anæmia A case of infectious mononucleosis showed infiltration of the sinusoids with immature members of the white-cell series. Typical Gaucher cells were demonstrated in a case of Gaucher's disease. A suspected instance of Banti's syndrome was found to have a normal liver on biopsy Diffuse hæmosiderosis has been demonstrated and used as confirmatory evidence for a diagnosis of acholuric jaundice in a patient who had no increase in red-cell fragility and subsequently underwent splenectomy with a satisfactory result

AMYLOID DISEASE

This condition may be extremely difficult to diagnose. Liver may be affected in the absence of renal changes Infiltration of the liver may be associated with normal blood biochemistry and liver-function tests. The Congo-red test is often normal or equivocal (Steinmerman and Auerbach 1944)

CASE 5 —A clerk, aged 29, was in 1941 found to have an intestinal ileosigmoid fistula of unknown ætiology There was hepatomegaly, the Congo-red test was positive, and the urine showed albumin and casts In November, 1941, an ileocæcostomy was performed, but it proved impossible to close the fistula A liver biopsy made at operation showed heavy infiltration with amyloid

In November, 1943, the patient was readmitted to hospital. The diarrhœa had persisted, there being 4–5 motions a day Otherwise he felt well and had gained weight The liver was just palpable The urine was free of albumin Urea clearance was 83% of normal The results of the hippuric-acid, galactose-tolerance, and bromsulphthalein tests were all normal The Congo-red test showed 50% retention of the dye in the plasma 60 min after injection. This figure is just within normal limits It was desired to know whether there was still amyloid disease in the liver Aspiration liver biopsy (fig 4) showed that there was still infiltration with amyloid, although this was considerably less coarse than in 1941

The other two cases of amyloid disease studied were associated with pulmonary tuberculosis, a positive diagnosis was made by liver biopsy

KALA-AZAR

In the tropics splenic and liver puncture are commonly used in the diagnosis of kala-azar. The specimens obtained are usually smears of blood from the liver or spleen which may or may not contain the parasite. Aspiration liver biopsy can show not only the Leishman-Donovan bodies but also the characteristic liver histology, which may itself be almost pathognomonic.

CASE 6 —A soldier, aged 28, had served in the North African and Sicilian campaigns On return to England he complained of rigors, malaise, nausea, and vomiting The liver and spleen were enlarged There were enlarged axillary and inguinal lymph-nodes There was an irregular pyrexia of 100–102° The patient was anæmic, the erythrocytes being 3,300,000 per c mm and the hæmoglobin 57% (Haldane). The leucocytes were 2850 per c.mm, with a relative lymphocytosis and 15% immature polymorphs No parasites were obtained by sternal or splenic puncture The fever did not respond to sulphathiazole or mepacrine, and a provisional diagnosis of kala-azar was made The patient received ten injections of stilbamidine (total 1 37 g) He was referred to Hammersmith Hospital for aspiration liver biopsy The biopsy specimen (figs 5 and 6) showed well marked portal zonal infiltrations as well as scattered islands of endothelial proliferation in the lobules. These were very numerous. Leishman-stained sections showed the characteristic Leishman-Donovan bodies in the reticulo-endothelial proliferations. It is interesting to note that parasites could still be demonstrated after the course of stilbamidine

The other two instances of kala-azar showed the same general liver histology as case 6. In one the parasites could not be demonstrated In the other they probably existed in a degenerate form In both these cases smears of liver blood would probably have been classed as negative The characteristic histological picture shown by liver biopsy gives useful evidence in distinguishing this condition from other causes of hepatomegaly or splenomegaly

MISCELLANEOUS CASES

This group comprised a wide variety of diseases. There were 34 cases in this group which were suspected on clinical and laboratory grounds to have a liver lesion most often cirrhosis, but showed normal liver histology

indicates the frequency with which liver disease is misdiagnosed. Moreover, "hepatic insufficiency" is often postulated in general diseases, especially those, such as rheumatoid arthritis, which are of obscure etiology. Therapeutic agents—e.g., mepacrine—have, largely on the basis of massive dosage in animals, been held to cause liver lesions. Aspiration liver biopsy has been of value in showing the absence of liver damage in these and other conditions.

Summary

The technique of aspiration liver biopsy is described. Difficulties and risks are discussed.

An analysis of 204 biopsies is presented. Representative cases have been selected, and described to demonstrate the diagnostic use of the method.

I am indebted to the Medical Research Council for an expenses grant for technical assistance; to Major-General A. G. Biggam, Lieut.-Colonels W. R. M. Drew and W. H. Hargreaves, and Major James Marshall for many of the cases studied; to Mr. J. R. Baker and Mr. J. C. Griffin for the histological preparations; to Mr. E. V. Willmott for the photomicrographs; and especially to Prof. J. H. Dible and Dr. J. McMichael for their assistance and criticism.

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RETROPULSED INTERVERTEBRAL DISK PRODUCING FROIN'S SYNDROME

REPORT OF A CASE

R. R. HUGHES, M.B., LPOOL, M.R.C.P.
MAJOR, RAMC, MEDICAL SPECIALIST AND GRADED NEUROLOGIST

WHILE a minor degree of spinal block is commonly associated with a retropulsed intervertebral disk, this case is of interest in that the block was apparently complete.

A man, aged 33, apart from two previous attacks of pleurisy had been quite well until the onset of his present trouble. The condition began in November, 1943, with pains in both buttocks; during the next few weeks the pains gradually spread down the back of both legs and calves to the ankles. They were aching in type and were associated with a stabbing pain of the same distribution on coughing. About the time of onset frequency and urgency of micturition lasted for about two weeks and then completely cleared. In January, 1944, the patient noticed a numb "dead" sensation over the left buttock, the back of the calf, and the outer side of the left ankle and foot. At the same time the legs became weak, and he could only walk with difficulty, being unable to move the toes of his left foot.

On admission to hospital in February 1944 his most trouble some symptoms were the numbness and weakness of the legs; pain was still present but not severe. He could walk only with difficulty by holding on to the foot of the bed. On examination there was loss of the normal curve of the lumbar spine and gross limitation of movement in all directions; there was no scoliosis. There was also generalized tenderness on deep palpation in the lumbosacral area but no tenderness on pressure over either sciatic nerve. The loss of muscular power was due largely to weakness of the flexors and extensors of the ankle joints and toes on both sides, but no muscle was completely paralysed. The ankle jerks were both absent, knee jerks were normal, and plantar responses were flexor. Sensation of pinprick and light touch was slightly impaired over the outer aspect of the left calf and the dorsum and outer part of the sole of the left foot. Straight leg raising was limited to 45° on both sides. Apart from the above findings his nervous and other systems were normal.

Radiography of the lumbar spine and pelvis revealed no abnormality. On insertion of a needle into the subarachnoid space between the 4th and 5th lumbar spines the cerebrospinal fluid pressure was found to be so low that it could not be measured with a manometer. On abdominal compression the rate of drip of fluid from the needle slightly increased, but on jugular compression the rate did not change. Only about 1 c.cm. of fluid could be obtained on which the pathologist reported as follows: 2750 red cells and 10 lymphocytes per c.mm., protein 280 mg. per 100 c.cm., fluid slightly xanthochromic and clots spontaneously. A needle was then inserted between the 2nd and 3rd lumbar spines; here the cerebrospinal fluid pressure was 50 mm. and increased to 80 mm. on jugular compression. The Wassermann reaction was negative in both blood and CSF.

The patient was transferred to an EMS Neurosurgical Unit for further investigation and treatment. Radiography after intrathecal injection of Lipiodol demonstrated the upper level of the block to be about the centre of the body of the 4th lumbar vertebra. Laminectomy was performed on March 8, 1944, and on palpation of the dural sac a large mass could be felt mainly on the right side at the level of the disk between the 4th and 5th lumbar vertebræ. On further exploration this proved to be sequestrated disk material, which was easily removed. It measured 3.5 × 1.4 sq. cm. and weighed 1.4 g.

Convalescence was uneventful and was accompanied by rapid improvement in the motor and sensory changes.

I wish to thank Colonel W. H. O. Riordan, RAMC, for permission to publish notes on this case, and Mr. F. B. C. Hughes, first assistant to an EMS Neurosurgical Unit, for kindly supplying details of the operative procedure and findings.

INTERDIGITAL RINGWORM

TREATED WITH SOLUTION OF SULPHURATED LIME

THEODORE JAMES, M.B. CAPETOWN
SQUADRON LEADER, RAF

A PATIENT who had "tried everything" for an intractable tinea cruris which he had had more than six months, was treated with Vleminckx's solution (liquor calcis sulphuratæ, *BPC*). After four days' treatment the condition was cured and the patient so pleased that on his own initiative, he tried the solution on a long standing ringworm of his toes, which also cleared up in less than a week. This unexpected result led me to try this solution for all cases of interdigital ringworm which subsequently came under my care. Until then I had used various medicaments according to their availability, but only when Vleminckx's solution was used were the results uniformly gratifying.

In warm climates interdigital ringworm is especially prevalent and, although only occasionally almost crippling, always a nuisance because of persistent irritation about and between the toes. I have treated successfully, at a conservative estimate, 100 cases ranging from slight, of a few days' duration, to those that had been neglected for months and on which a secondary infection had been imposed. In a number of instances the sole, the dorsum, or both surfaces of the foot had become involved, and the patients were kept off their feet until cured. In only one case did dyshidrosis of the hands an unusual complication of ringworm of the feet develop, and this appeared during treatment of the feet. This complication became aggravated after the ringworm had been cleared. The shortest treatment for the slight condition was three days, and the longest for the severer ten days. There were no facilities for microscopical identification of the infecting agent.

The formula and directions for dispensing liquor calcis sulphuratæ (Vleminckx's solution) are given in the British Pharmaceutical Codex (1934) but under service conditions the following method proved effective. Quicklime, 25 g., was slaked with an equal quantity of water, 50 g. of sulphur

sulphur was added, and then more water to a total volume of 1 litre The mixture was then boiled until it was reduced to two thirds of its original volume, when it was allowed to cool and the solid to settle, and then the supernatant fluid was decanted Distilled water was not necessarily used, nor was the container kept always completely filled Two distinct advantages in the manufacture of this agent commend themselves to Service medical officers the availability of the ingredients and the ease of preparation It is also inexpensive

METHOD OF TREATMENT

The feet, especially the interdigital clefts, were thoroughly washed with soap and hot water and dried, and any necrotic and macerated epidermis was removed with forceps Any vesicles were opened If enough of the solution was available, the feet were soaked in it for ten minutes A number of feet could be treated with the same solution, or the affected part was swabbed with a pledget of cotton-wool soaked in the solution The treatment was repeated twice daily Sometimes, if the skin was raw, the solution stung when first applied; but this was momentary and did not adversely prejudice the patient

Soon after the beginning of treatment all the patient's footwear, including socks, stockings, boots, and shoes, was treated with formalin according to the method of Berberian (1938)—i e, they were damped with water and spread in an enclosed drawer or its equivalent in which was placed an ounce or so of formalin in a dish or saucer When the articles were numerous, some other appropriate enclosed space could usually be found The articles were left in the formalin for six hours In this way the fungus suspected to be on the footwear was considered to be destroyed This treatment of the foot wear is very often neglected, the fact that this neglect may be an important factor predisposing to relapses should therefore be emphasised. Once the treatment for the ringworm was started, the disinfected footwear was again allowed to be worn.

Prehn's (1938) powder (salicylic acid 5 parts, menthol 2 parts, camphor 8 parts, boric acid 50 parts, and starch 35 parts), if available, was used as a prophylactic dusting powder for the two weeks following the end of treatment In warm climates Prehn's powder, apart from its fungicidal properties, was found to be an excellent cooling foot-powder by those who had to do much marching.

I have not had occasion to treat the same patient twice for interdigital ringworm in at least 100 cases, and cases were clinically cured in from 3 to 10 days. There were no relapses during the time they were under my supervision, which time was as short as a few weeks or as long as several months, although reinfection in Service life is very likely The only disadvantage of the solution is its strong unpleasant odour, which does not, however, attach itself for more than a few minutes to the part being treated

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Medical Societies

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION

AT the 104th annual meeting on Sept 5, with Lieut-Colonel A A W. PETRIE, the president, in the chair, a symposium on

Ageing and Senility

was opened by Dr AUBREY LEWIS He showed that the proportion of the population in the older age-groups admitted to mental hospitals in England and Wales in a first attack of mental disorder had risen steadily in the last fifty years, except for a large fall in 1918–30 immediately following the war years 1914–18 From 1930 onwards a significantly rapid rise had again taken place and was apparently continuing now This unexpected drop in the post-war years was probably due to the increased number of elderly persons cared for, during these years, in public-assistance institutions other than mental hospitals Thus in 1932 two-sevenths of the inmates of London County Council workhouses were labelled as mentally affected and one-eighth as cases of senile dementia These demented old people ought to be sent to mental hospitals, because in the workhouses there was not enough specialised nursing for them The rise in incidence of first admissions did not affect the sexes equally, the women easily outnumbering the men. Dr Lewis gave figures showing a much greater rise of incidence of first-attack admissions in New York and Massachusetts for both sexes but with a greater number of males the opposite of what was found in England The differences were probably attributable to the difference in social conditions in the two countries In conclusion Dr Lewis said that the centre of this problem of psychiatry was the process of normal ageing, which needed much more study

Miss H GOLDSCHMIDT read a paper on the social aspects Her material consisted of 25 men and 25 women in each of four London groups of old people inmates at Tooting Bec a Darby and Joan club, old people living singly, and a settlement for old people She analysed the mental conditions found in each group separately and gave illustrative examples Attention was drawn to five major factors for research in the study of mental deterioration in old people

The first of these was social integration—the degree to which an old person fitted in not so much with the rest of his household or his fellow inmates as with the world at large The effect on social integration of war conditions, character and temperament, excessive consumption of alcohol, and the changed attitude of children towards their parents was examined In this connexion there was a tendency today for the children not to look after their aged parents A second factor was the effect produced by the type of work, manual or other, which was dropped when the aged person retired This did not appear to be correlated with any special type of mental breakdown On the other hand, being forced to give up active work of any kind often led to a sense of frustration at having to make way for the younger generation The majority of mentally affected old people had not taken up any other work or hobby on retiring A quarter of them were financially insecure, and a large proportion had been living on a deficient diet A third factor was infirmity, physical or other An example of the other kind of infirmity was nationality, if the person could not make himself understood in English or if he was not completely accepted by the English community This produced a sense of inferiority War conditions, apart from injuries, formed a fourth factor, including air-raids and loss of home Critical occurrences not due to war conditions, such as enforced change of habits and accommodation and loss of spouse, were also considered under this heading The fifth factor, last but by no means least, was the previous mental health Defects of personality were found in more than half of either sex at the Tooting Bec institution for old folk

The Darby and Joan club was beneficial to old people in that the possibility of social integration was enhanced by the facts that there were 1100 members and that the club was open six days in the week The wish, expressed by most of this group, to live alone rather than with their children was due to a sense of inadequacy in relation to their children as well as to a feeling of independence arising from their club membership. Miss Goldschmidt suggested the use of a non-residential advisory centre for the ageing and aged, staffed by doctors, psychologists, and social workers familiar with the problems of this period of life This centre should be run on the lines of a child-guidance clinic, and one of its main functions should be to interpret the particular needs of the old to the young and vice versa

Mrs MARGARET EYSENCK, speaking on the psychological aspects, reviewed evidence which shows that mental ability, as measured by intelligence tests, declines slowly after the age of 25 and more rapidly after the age of 50–60 This decline is more rapid in the dull and less rapid in the bright adult and takes place at different rates for different abilities Further, with age the ability to learn also declines, and in consequence feelings of inadequacy and inferiority often arise. Increased ar

also brings with it a general withdrawal from all types of activity

Dr DEREK RICHTER reported results of an investigation of biochemical changes in senility Senility, he said, had three components—chronological ageing, physical deterioration, and mental deterioration. He set out to discover if any biochemical factors were correlated with any of these three components A difficulty was that patients with senile dementia also had other senile changes. His material consisted of 2600 old people at Tooting Bec, and the three components were assessed in each case investigated Chronological ageing was easy to assess, physical deterioration was less so, but methods were devised for testing it which included measuring the response to making the subject walk up a certain number of steps To measure mental deterioration five psychological tests (so-called intelligence tests) were used He next investigated 75 selected cases by submitting them to biochemical tests, and found by statistical analysis that, although most of the biochemical findings bore no correlation with any of the three factors of senility already mentioned, the following statistically significant correlations were obtained:

(1) With chronological ageing the basal metabolic rate tended to fall and the blood sugar level to rise
(2) With physical deterioration the erythrocyte sedimentation rate rose (probably owing to toxæmia) and the vitamin C level was low
(3) With mental deterioration there was a diminished clearance of urea, accompanied by an increased amount of non protein nitrogen in the blood (effects attributed to impairment of renal function, probably by the same factor that impaired the brain) and the choline esterase level in the serum was low, possibly owing to the lowered physical activity in demented persons.

Dr Richter emphasised the importance of mental rather than physical deterioration in senility, and the importance of prevention rather than palliation—i.e, of research rather than homes for the aged

The PRESIDENT summed up the four papers, and in the discussion which followed Professor D K HENDERSON said he had noticed in recent years a great increase in incidence of the Alzheimer-Pick group of pre-senile mental disease He regretted that the speakers had not mentioned heredity, which he considered to be an important factor in senile mental deterioration.

TUBERCULOSIS ASSOCIATION

AT a meeting in Bristol on Sept 6–7 with Mr J E H ROBERTS the president, in the chair Prof R H PARRY, MOH for the city gave an opening address in which he said that its public health services have grown eight fold in ten years, so that now about 10 000 people attend health centres each week. Newer knowledge of tuberculosis must be available to everyone; and since it is a social disease, he thinks it would be a mistake to detach tuberculosis units from the wider field of social medicine

TUBERCULOSIS AND THE EYES

Dr WILLIAM STORIE (Oxford) said that in European countries chronic iridocyclitis is often labelled tuberculous, but this is not confirmed Sarcoidosis may be a variant of tuberculosis—an unusual reaction perhaps to an attenuated or even a non human bacillus The disease is often seen at eye hospitals, with eye symptoms; radiography of the chest usually shows enlarged mediastinal glands or nothing abnormal at all Ocular lesions develop most often in the secondary phase of tuberculosis, when there is an allergic response to circulating tuberculo-protein and usually a positive tuberculin test This is probably a factor in phlyctenular conjunctivitis, though there are others—ill balanced nutritional state and often chronic infection of the upper respiratory tract In uveitis the whole vascular tunic of the eye is affected and the cause may be more often related to sarcoidosis than to tuberculosis Many patients recover eventually, but a number go blind

Prof E. RIST (Paris) reported 7 cases of primary tuberculosis of the conjunctiva which recovered Dr BRIAN THOMPSON (Middlesex) said that in giving a course of tuberculin, sooner or later a dose is reached beyond which focal or general reactions will develop Dr J V HURFORD (London) supported Dr STORIE's views on phlyctenular conjunctivitis which develops, he said, in only 1 or 2% of children with primary tuberculosis In replying Dr STORIE mentioned that tuberculin can be useful in lupus, though it is too slow in comparison with other methods of treatment

TREATMENT OF PRIMARY TUBERCULOSIS

Dr PETER EDWARDS (Cheshire) outlined the procedure at Cheshire Joint Sanatorium in dealing with nurses who have shown tuberculin test conversion—so far, 48 of 70 Mantoux negative entrants In 7 years there were 10 cases of illness due to primary or postprimary shadows, but, except for pleural effusions in 3, none relapsed He considers that no Mantoux negative nurse should be excluded from work When conversion occurs the case should be treated according to the symptoms. If the girl is symptomless, she should go to bed early for a time If the ESR is increased she should go on half-duty for a month If she has enlarged glands or primary complex she should go off duty for a month and then if the glands are regressing on to half-duty for 3 months. If she is clinically ill, she should have strict sanatorium routine

Dr W SNELL (London) doubted the wisdom of employing Mantoux negative nurses in sanatoriums; Professor RIST also took this standpoint In Paris he said, Mantoux negative students or nurses are kept out of tuberculosis wards, for the primary infection is occasionally rapidly followed by phthisis Dr BRIAN THOMPSON described work he is doing on so-called idiopathic pleural effusions. About a fifth of the cases (mostly young adults) have primary disease, and something like 20% subsequently develop phthisis Dr F RIDEHALGH (Leeds) also thought there is a definite risk for the Mantoux negative nurse, but if she is rejected by the sanatorium he said, she should not nurse in the general hospital Several other speakers supported the opposite view, Dr STEPHEN HALL (Middlesex) thought that the girl who is not a nurse runs six or seven times more risk of contracting tuberculosis than the girl who is

CHEMOTHERAPY IN EMPYEMA

The PRESIDENT reviewed the characteristics of various empyema fluids and pointed out that anaerobic organisms may be missed if only aerobic cultures are made The fibrin deposit in empyema may eventually cripple one side of the chest and cause it to be "frozen" The three objects in treatment are abolition of infection obliteration of the pleural cavity by expanding the lung and restoration of respiratory function The quickest method of fibrin removal is by rib resection, the clot being turned out In the young child and in acute streptococcal infections, this may be done after preliminary chemotherapy, but it should be the first measure he said, in pneumococcal and staphylococcal cases. With penicillin treatment, an empyema may quickly become sterile, but it is wise to give at least three further injections before discontinuing the penicillin The organism must be tested for sensitivity; some abnormally resistant staphylococci require very large initial doses, otherwise they become completely resistant In all Mr Roberts's cases rib resection was necessary at one time or another Penicillin seems to be of great value in actinomycosis For penicillin resistant organisms, 2% Phenoxetol' has been used with varying success. For tuberculous empyemata Azochloramide-T' and 'Promanide' are in use but it is hard to separate their effect from that due to early and frequent aspirations

Prof R PILCHER (London) felt that there is no need to delay treatment until thick pus has formed The ability of penicillin to sterilise the pleura if the organism is sensitive, is not the only therapeutic factor it is also necessary to clear the pleural cavity of fibrin and to keep it clear This must be done early by rib resection and removal of fibrin under direct vision, followed by closure of the wound Breathing exercises must be done to restore function Sulphanilamide injected into the pleural cavity may deal with penicillin resistant organisms Secondary infection may be avoided by keeping the pleura closed after the initial toilet and by repeated aspiration The dose of penicillin depends on intervals between aspirations and whether a systemic effect is

desired Intrapleural penicillin will remain effective for a maximum of 4 days

Mr LIBERO FATTI (Middlesex) quoted cases treated at Hillingdon with intrapleural penicillin given every 12–24 hours through a thin catheter Fibrin could often be washed out quite easily through the catheter He considered that treatment should be continued for 7–10 days after the pleura becomes sterile A bronchopleural fistula often closes under penicillin treatment Dr L E HOUGHTON (Middlesex) thought azochloramide-T of value in tuberculous empyema, though prophylaxis is better treatment In spontaneous tuberculous pneumothorax, penicillin may be used prophylactically Dr W. FOWLER (LCC) thought frequent aspirations with avoidance of track sinuses especially important in tuberculous empyema

TUBERCULOSIS IN PRISONERS-OF-WAR

Lieut -Colonel W H B BULL, NZMC, said that most prisoners-of-war in Germany would remember the period as bounded by two horrible marches, with five years' boredom in between He described the successive German hospitals used for treatment of tuberculosis from early in 1941 onwards The final choice was Elsterhorst, which started in February, 1942, had fairly good accommodation and facilities, though relations with the Germans were never good there Repatriation started in October, 1943, but the parties of returning prisoners were never accompanied by doctors or orderlies The general standard of treatment of sick prisoners-of-war in Germany was bad, though often good on paper Most young German doctors were Nazis first and doctors some way after. Red Cross parcels supplied both food and equipment, and were probably responsible for the survival of at least half of all prisoners-of-war

TUBERCULOSIS IN EUROPE

Professor RIST said that during the occupation assessment was difficult, but that 21% of deaths reported from prisoner-of-war camps were probably due to tuberculosis during the period of July, 1941, to December, 1943, and 18% of French prisoners released for sickness were consumptive Rapid consumption affected many of the civilians gaoled in France Among the factors influencing tuberculosis incidence in the population were displacement of people, increased opportunities for contact, undernutrition, and partial collapse of preventive and therapeutic schemes Immediately on the French armistice, rations were officially reduced to 1500 calories daily, but amounts were often much less, especially in the cities—where in 1940–41 the bulk of food consisted of edible roots and vegetables and about 200 g of bad bread The black market helped only the well-to-do Hunger-œdema and pellagra were quite common The increase in the tuberculosis death-rate was in mainly urban areas, varying from 30 to 86%, in rural areas it actually fell The disease has become strikingly severe, and acute forms are commoner The morbidity figures have gone down consistently, but greater numbers have died, often after a very short illness

Dr LUCIEN WYBAUW (Brussels) said that rations in Belgium during 1940–44 varied between 1900 and 1300 calories daily Tuberculous patients got a double ration, theoretically; but the poorer classes could not pay for it The numbers of cases reported from dispensaries rose from 42,000 in 1940 to 131,380 in 1943 Acute cases became commoner, and so did relapses, and tertiary forms among children

Dr HEYNSIUS VAN DEN BERG (Amsterdam) was prevented from attending and his paper was read for him In the Netherlands, tuberculosis mortality (all forms) increased from 41 to 70 per 100,000 from 1939 to 1943, and the increase was even greater in Amsterdam Morbidity (Amsterdam) increased proportionately Pulmonary tuberculosis showed a greater increase in men than in women In prisons and concentration camps the increase appeared to be due largely to new infections In the population, however, the increase was probably due to endogenous reinfection or flaring up and the illness was usually more acute and rapid than in peace-time Probably the main factor was nutritional From December, 1944 rations sank as low as 500–600 calories daily with little protein and fat In May, 1945, they were 250 calories a day Hunger-œdema and exhaustion were common

Reviews of Books

Gout

JOHN H TALBOTT, MD, associate in medicine, Harvard University (Oxford University Press Pp 126 12s 6d)

IN his foreword Dr Henry A Christian, editor of the *Oxford Loose-Leaf Manual* of which this book is a constituent, points out that gout has been generally considered to be an unusual ailment in the United States, yet Hench has estimated that this diagnosis should be applied to at least 5% of all patients at the Mayo Clinic suffering from arthritis, and the percentage is valid throughout the United States—accounting, that is, for about a third of a million among the 7 million sufferers from chronic rheumatism Since gout is a traditional malady in Great Britain, we may speculate what a like assessment would reveal here Few examples seem to be reported at present, but that may be because we fail to suspect gouty arthritis until advanced tophaceous changes in the joints have appeared

The book outlines modern research, but gives the impression that nothing more definite is now known about the ætiology of this ancient disease than the older physicians knew Garrod, in 1876, said that gout is probably one of the earliest diseases resulting from the luxuries of civilised life Alexander of Tralles in the 6th century used colchicum successfully in its treatment, Scheele found uric acid in the urine in 1776, and Wollaston isolated uric acid from tophi in 1787 We know that hyperuricæmia is the essential factor, but still cannot explain the dysfunction which increases the concentration of urate in the body fluids and deposits it in the tissues Garrod's theory of diminished excretion by the kidneys is not supported by modern estimations of renal function, though prognosis certainly depends on the state of the renal vessels The essential problem remains, and the clinical treatises of our distinguished predecessors—the Garrods, Dyce Duckworth, Luff and Osler, and the great Sydenham himself—are still supreme Dr Talbott supports the opinion of Bauer and Klemperer[1] that there is little reason to consider gout a disease of "persons who are habitually intemperate whether it be in regard to alcohol, to sex activity, or to food" He adds that the evidence is very slight for the ascription to the gouty diathesis of bronchitis, dyspepsia, iritis, gravel, cystitis, psoriasis, phlebitis, glycosuria, pharyngitis, migraine, and neuritis No complication, he says, should be called gouty unless it is associated with deposition of urate

X-ray photographs preponderate among the 56 fine plates, but he insists that it is dangerous to rely on radiographic evidence, and enumerates conditions giving similar pictures, including rheumatoid arthritis, psoriatic arthritis, chronic trauma, Boeck's sarcoid, syphilis, multiple ganglionata, multiple myelomata, enchondromatosis, hyperparathyroidism, Paget's disease, and generalised calcinosis He notes the familiar confusion of acute gout with cellulitis and advises that, before operation is done in any doubtful case, the uric-acid content of the serum should be estimated

Diseases of the Nervous System

(4th ed) F M R WALSHE, MD LOND, FRCP, physician i/c neurological department, University College Hospital, London (Livingstone Pp 360 15s)

IN the new edition of this deservedly popular book the chapters on the peripheral nerve lesions, herpes zoster, cervical rib, sciatica, and protrusion of the intervertebral disk have been recast, and new matter on the nature of ætiology, and on the concept of psychosomatic illness, has been included The section on sciatica perhaps leaves the impression that diagnosis of the cause of sciatica is more difficult than it usually is, and no mention is made of examination of the cerebrospinal fluid in sciatica nor of the help which may be obtained in diagnosis from straight X-ray examination of the lumbosacral spine.

Psychological disorders can scarcely be dealt with adequately in a textbook on nervous diseases, and this section is the least satisfactory in the book The diagnostic aspects of the psychoneuroses are adequately dealt with, but the nosology is somewhat old-fashioned

1. Bauer, W, Klemperer, P *New Engl J Med* 1944, 231, 631, and see *Lancet*, Feb 10, 1945, p. 187.

THE LANCET

LONDON SATURDAY, SEPTEMBER 29, 1945

Action against Rheumatic Diseases

A NEW Minister is surveying the health of the coun y, and it is probable that he will place chronic rheumatism" on the list of high priorities It ould be natural for an ex miner from the Ebbw Vale to take a realistic view of Public Enemy No 1 of the oal (and other) industries The necessary first step, owever, was taken by his predecessor Mr WILLINK, hen in May, 1944, he added a sub committee on ronic rheumatic disease to his Standing Medical lvisory Committee, and instructed this body to amine with all speed the practical possibilities fighting rheumatism more effectively This ey did, under the chairmanship of Prof HENRY OHEN, and their plan in essentials followed the one it forward by the Empire Rheumatism Council in 941 and published over the signature of Lord IORDER as *Rheumatism a Plan for National Action* The new proposals had to be put aside for the moment ecause of the lack of medical personnel, but the eriod of cold storage, we may hope, is soon coming to n end, and already, we are told the Government's lecision to tackle not only diseases that kill but also hose that cripple has acted as a stimulus to other nations In the words of Dr RALPH PEMBERTON, president of the Pan American Rheumatism League, "it will influence thought everywhere"

The plan is based on the need to concentrate the nore specialised facilities which are essential for liagnosis or treatment in many early cases of chronic heumatism and arthritis For this purpose the reation of a special department in a principal hospital n every region is advocated This will be in charge of a physician who will have access to all the hospital esources, such as radiography, laboratory facilities, nd (not least) the opinion of his colleagues—notably he orthopædists Around this regional nucleus there ll be an outer circle of smaller clinics whose staff and quipment will be less specialised these will serve ainly as treatment centres and will refer their more bscure diagnostic problems to the hospital centre uch a scheme has the merit of making full use of the ervices of physicians with special knowledge and experience of "rheumatology," and of avoiding additional pressure on the physical medicine depart nents of hospitals It should also provide favourable rroundings, and large opportunities for much needed search under university auspices An experimental ial of the scheme, early this year, in one or two ctors of the Emergency Medical Service did not eet with great success, because both medical and ssing staff were insufficient but we understand t in Manchester a special committee has recom mended that an institute shall be set up for the study of bone and joint pathology in the rheumatic diseases, while in Liverpool and in Leeds arrangements are to be made between the voluntary and municipal hospitals which should result in diagnostic centres being established, with beds in which patients can stay as long as may be necessary, and in which research will be undertaken under the auspices of the professor of medicine In London no teaching hospital has yet followed the example of the West London Hospital, which in 1938 set up a department on lines similar to those of the present scheme, but at least one of the Big Twelve now has this project under consideration

The prominence of chronic rheumatism as a cause of sickness and absence in industry has attracted the attention of other Government departments, including the Ministry of Labour, and the Ministry of Fuel and Power, and of the Industrial Health Research Board There is reason to hope that the universities, through their teaching hospitals, will in the near future join in the establishment of the special centres proposed by the Ministry of Health and that voluntary organisations interested in medical research will support investigation in such centres We must now try to fulfil the prophecy of the *Times* when the campaign against rheumatism opened "As it grows in strength it will spread over the whole country, and from its success the nation is likely to reap substantial advantage"

Surgery in Ulcerative Colitis

IT is to be hoped and indeed confidently expected that the surgical treatment of ulcerative colitis is but an interim measure which will be discarded when a more thorough understanding is reached of this distressing complaint Its etiology is still far from clear There is a stage of the disease when the picture is one of infected ulceration, but the lack of confirmation for BARGEN's diplococcus, and the failure of attempts to find other specific causative agents have cast doubt on infection as a prime factor, though treatment with the "sterilising" sulphonamides, especially when combined with penicillin,[1] has sometimes been successful—perhaps, as it does in amœbic dysentery, because it holds secondary invaders in check That deficiency may play a part is supported by MORTON GILL's[2] experience with fresh and dried pigs' intestine, both of which, given by mouth, led to improvement in some cases The association of the complaint with emotional instability, and the tendency of emotional crises to precipitate recurrences, suggest some inherent sensitivity or diathesis, while allergy has also been called on to account for the patients susceptibility, although the stimulus to which they over react is not apparent[3] None of these avenues of investigation looks like leading to a surgical goal but while they are being explored, surgery, though difficult and uncertain, can tide many patients over a bad patch prevent others from relapsing and save the lives of some

Surgery has been adopted for three purposes in ulcerative colitis (1) to promote easy access of medicaments and wash-out fluids to the colon, (2) to rest the inflamed and ulcerated bowel and (3) to extirpate the seat of the disease The first of these has largely been superseded, for even if it is desirable to wash out the bowel, which is doubtful, this can be done adequately from the rectum although not with the same certainty as through an appendical or cæcal opening If the appendix is unsuitable and cæcostomy is performed into potentially or actually diseased bowel the results may be horrible for the patient in addition to passing

1 Hargreaves W H *Lancet* July 21 1945 p 64
2 Morton Gill A *Ibid* Aug 18 1945 p [illegible]
3 Hardy T L *Ibid* 1945 i 519 553

a running stool per rectum may have a continuous excoriating discharge from the cæcostomy.

Rest to the bowel can be brought about only by disconnecting it from alimentary function Since the whole colon may be or become the seat of the disease, disconnexion must be done above this level—that is, in the terminal ileum CORBETT,[4] in summarising the case for ileostomy, emphasises the too little recognised point that an established ileostomy is no more difficult to manage, and often no more fluid in its discharges, than a colostomy He mentions an operative mortality for ileostomy of 30%—a formidable figure. His cases are too few to assess late results BARGEN and his colleagues[5] have analysed 185 cases submitted to ileostomy and confirmed the distressing operative mortality (rising to 60% in fulminating cases), of 130 cases that survived the operation for six months, 51 had severe and frequent recurrences, of which 26 died in a recurrence Unfortunately the extreme variation in severity characteristic of the disease makes all such results difficult to evaluate It is probable that any series of cases will include more than one entity, and that different series will contain different proportions of each entity The severe cases commonly operated on are so desperate that the surgical mortality may not be high by comparison with other measures, but it is difficult to get an exactly comparable control series No doubt a patient partially moribund from ulcerative colitis, with all the evidence in a distended silent abdomen that infection is seeping through the bowel-wall, can recover without surgery, but it is more likely he will die either way Though their evidence might not satisfy the statistician, most surgeons who have practised ileostomy are convinced that it has arrested attacks, sometimes even in the fulminating stage, and that sometimes it has arrested the disease itself Certainly the principle of rest is hallowed by reason and wide experience with analogous ailments. CORBETT mentions the inadvisability of handling the large bowel at operation in these cases —sound advice, for the bowel wall behaves like damp blotting-paper and manipulation may lead to rapid perforation or may so increase the permeability of the affected bowel that a purulent peritonitis spreads out like wildfire To hook out the terminal ileum with a finger is all the intra-abdominal manipulation permissible.

Any surgeon who has studied acute cases at autopsy will have had his courage shaken by the appalling extent and malignancy of the gangrene of the mucous membrane and will hardly be surprised at some of the X-ray pictures of the colon in a quiescent stage after ileostomy—long, thin, almost wholly inactive rigid tubes, varying perhaps a little in calibre but never distensible That such a colon could function again is out of the question, although it must be emphasised that this is only one type of case MAINGOT[6] suggests that a really early ileostomy might prevent irreversible changes taking place in the colon, and therefore permit subsequent restoration of normal bowel continuity. This may well be true, but to do such an operation before the characteristics and severity of the individual case have been revealed would often be to do it unnecessarily Moreover, the results of early ileostomy with restoration of continuity can be assessed only in terms of very long periods and by comparison with the long remissions which may occur spontaneously, and when continuity is restored the patient and surgeon may be oppressed by the thought of the poised sword of Damocles—not that an active ileostomy completely removes the threat of recurrence. Most surgeons agree that there is but a slender chance of an ileostomy done late in the disease being closed, whether the colon is or is not removed, "an ileostomy," as R B CATTELL puts it, "is the price that some patients must pay for life"

The prime indication for removing the colon is recurrence of the disease in the presence of an ileostomy This is a dangerous procedure, but then this is a dangerous disease It must, of course, be done in as quiescent a phase as possible Generally speaking, the rectum can be left behind, even if perianal fistulæ are present The rectum is seldom so severely affected as the colon, and its disconnected stump fairly readily heals, although reinsertion of the ileum into the rectum, besides being difficult and dangerous, is liable to produce recurrence in the rectum

Any of these measures may profitably be accompanied by blood-transfusion, or transfusion may be given apart from surgical treatment Even in the absence of anæmia—though it seldom is absent when the hæmoconcentration of chronic dehydration is taken into account—transfusions confer a striking temporary and sometimes permanent improvement

Gastric Cancer and Pernicious Anæmia

THE observation that gastric cancer and pernicious anæmia can coincide in one patient is an old one a case was reported by QUINCKE in 1876, and many others have been recorded since But it was not until a gastric lesion was recognised as an essential part of the pernicious-anæmia syndrome that it occurred to anyone that the combination is more than accidental. At that time many observers, particularly HURST and FABER, attributed the achlorhydria of pernicious-anæmia to a gastritis, and it was also supposed that gastritis precedes cancerous changes in the gastric mucosa Most of the gastric cancers in pernicious-anæmia patients were found in the pyloric area, and MEULENGRACHT'S experiments with pigs' stomachs showed that the anti-pernicious-anæmia principle is mainly concentrated in the pyloric part It seemed then that pyloric gastritis was the factor common to the two diseases, explaining why gastric cancer is seen more often in pernicious-anæmia patients than among the general population[1-3] This chain of evidence, however, has now been challenged at almost every link The more recent work on the histology of the stomach in pernicious anæmia, done with special precautions against post-mortem changes, shows simple atrophy without gastritis, affecting mainly the cardiac and fundal regions,[4] and gastroscopy confirms these findings[5] As for gastritis preceding carcinoma American surveys[6] suggest that gastritis is common after middle age and is no more closely associated with cancer than with other diseseas Lastly, MEULENGRACHT'S results with pigs' stomach do not apply

4 Corbett, R S *Proc R Soc Med* 1945, 38 277
5 Bargen J A, Lindahl, W W Ashburn, F S, Pemberton, J de J *Ann intern Med* 1943, 18 43
6 Maingot R *Lancet*, 1942, II 121

1 Strandell, B *Acta med Scand* 1931, suppl 40
2 Wilkinson, J F *Ibid* 1933, 80, 466
3 Conner, H M, Birkeland I W *Ann intern Med* 1933, 7, 49
4 Magnus, H A, Ungley, C C *Lancet*, 1938, I 420
5 Schindler, R., Serby, A. M *Arch intern Med* 1939, 63, 531 Hebb R *Amer J Path* 1943, 19, 43
6 Guiss, L W, Stewart F W *Arch Surg* 1943, 46, 823

an,[7] in whom the main source of the anti pernicious-anæmia principle is the upper two thirds of the stomach, not the pylorus

Nevertheless, it remains true that the patient with pernicious anæmia runs a special risk of developing carcinoma of the stomach JENNER[8] in 1939 reported gastric cancer in 4 4% of 181 patients—12 times the incidence among other people of the same age-range OEHRING and EUSTERMAN[9] in 1942 found 1 6% in over 1000 autopsied cases of pernicious anæmia, compared with 0 3% in all other cases of the same age-group KAPLAN and RIGLER,[10] examining 293 cases of pernicious anæmia coming to autopsy, found gastric cancer in 36, an incidence of 12 3% compared with 4% among a large group of other cases of similar ages Thinking that routine barium meals might lead to early discovery of gastric lesions, they began in 1939 to give their pernicious anæmia patients a barium meal every six months, and of 211 thus examined,[11] they have discovered 17 (8%) with gastric cancer, and also 5 (7%) with tumours (mostly polypi) which were classified as benign though some of them may have become malignant later (A recent barium meal survey of 2400 symptomless persons over 50 years old revealed only 3 gastric tumours.[11]) OLSON and BECK[12] at the Mayo Clinic state that of 31 treated cases of pernicious anæmia, 6 developed gastric cancer and 8 had gastric polyps, these were found 5½–6½ years after the pernicious anæmia had been diagnosed FRANK[14] of Melbourne has described 5 cases among 88 pernicious anæmia patients seen during 10 years, there was no close follow up and no special search for gastric lesions, so the incidence is uncertain, but his paper is interesting because of the full case records The gastric lesions were found 14, 9, 3, 8, and 7 years after the anæmia had been diagnosed

The figures quoted are mostly from the United States, and our impression is that the incidence in this country, when the few workers who can produce adequate series have time to publish them, will be found to be much less than 12% It is clear, however, that gastric cancer and pernicious anæmia are in some way connected, though the nature of the connexion remains obscure Modern treatment of the anæmia, by prolonging the life of patients of an age liable to cancer, naturally allows more of them to develop gastric cancer, but this does not explain why the incidence is so much higher than among other people of the same age It has been suggested that the factor causing the changes in the gastric mucosa of the upper two thirds of the stomach in pernicious anæmia also renders it liable to malignant change, and treatment of the anæmia allows this factor to act for much longer than it did in the past Against this are the facts that most of the cancers are pyloric in site, and that, judging by gastroscopy, liver treatment can restore the gastric mucosa to normal

The increased risk being known, how can we deal with it? The method of KAPLAN and RIGLER of having semi-annual barium meals may be practicable for small selected groups, but one large clinic in this country has over 1000 cases being followed, and 2000 extra barium meals each year would severely tax the X ray department The difficulty in clinical detection is the silence of the early stages, when dyspepsia is noticed, or when the anæmia, previously controlled by treatment, begins to increase, the lesion is only too often inoperable There is at present no easy answer, but it is evident that the possibility of gastric cancer must be constantly in the mind of those with pernicious anæmia patients in their care

7 Fox H J Castle W B Amer J med. Sci 1941 203 18
8 Jenner A W F Acta med Scand. 1939 102 529
9 Oehring P C., Eusterman G B Arch. Surg Chicago 1942 45 534
10 Kaplan H S., Rigler L G Amer J med Sci 1945 209 339
11 Rigler, L. G Kaplan H S Fink, D L. J Amer med Ass 128 4 8
12 St John F B., Swanson P C Harvey H C. Ann Surg 1944 119 ~35.
13 Olson S. W Beck F I Proc Mayo Clin 1943 20 74
14 Frank, T J F Med Melbourne Hosp clin Rep 1944 15 12

Annotations

THE HAPPY WORKER

OUR opinions, logical or otherwise, influence our behaviour as effectively as our environment does Has enough thought been given to the effect that the opinions of workers in industry may have upon their work? In a study of women working in factories[1] Mr S Wyatt suggests that this aspect of social psychology in industry has been largely neglected up to now An earlier investigation by the Industrial Health Research Board showed that a comparatively small proportion of women were responsible for the greater part of the time lost to production through sickness, and this further investigation was undertaken to throw light on the unequal distribution of sickness absence among a factory population Five groups of women from four factories each group consisting of the 50 women with the least sickness absence in six months and the 50 women with the most, were interviewed Attempts were made to relate the amount of sickness absence to factory or home conditions Although the original purpose of the investigation was only partially fulfilled, in that the difference in sickness absence between the two groups was not associated with equally clear-cut differences in other respects, a revealing series of opinions on factory and home conditions were collected

Industry at present leans increasingly towards large factory units and the subdivision of work processes, so that there is a progressive decrease in the interest of the work It is therefore important to assimilate the worker into the social life of the factory and into a social group to offset tedium "The presence of others doing the same kind of work," the report says, "is not only comforting but helps to divert the attention from the monotonous and irritating features of work" Of the women studied, 94% were satisfied with their fellow workers, but only 68% with their supervisors Only a small minority had any real knowledge of the supervisory staff above the rank of foreman and what contacts did exist were usually connected with grievances and disciplinary action Thus it is not surprising that 'many workers regard the shop manager as an aloof and superior being whose function is to blame and not to praise' Here is one field where the social life of the factory could be changed with advantage Women factory workers in general have the dullest and most monotonous jobs inflicted on them In three of the four factories women worked a three-shift system alternating weekly—surely an arrangement profoundly disturbing to human physiology Yet 80% of them were satisfied with the shift system though 'they seemed to be influenced by certain specific dislikes associated with each shift which made them think that a longer period on that shift would be unpleasant or even intolerable

High wages are by no means the only incentive to factory work Three systems of payment were used—

1 A Study of Women in War Work in Four Factories By S Wyatt assisted by R Marriott W M Dawson Norah M Davis D J R. Hughes and F G L Stock Rep Industr Hlth Res Bd Lond No 89 HMSO Pp 44 9d

day-rates, group piece-rates, and individual piece-rates Women working on individual piece-rates were the best paid but the least satisfied with the wage system, because of inequalities in rates or amounts of payment between different individuals Much more popular, though the wages were less, was the group piece-rate system, which appealed to the social qualities of coöperation, tolerance, and mutual help But by far the most popular system was the day-rate, although it was the worst paid · several women referred to the higher quality of work possible under this system where the speed of work is not the primary consideration It is interesting that 75% of women preferred day work to night work, despite its lower rates of pay. The value of an incentive beyond the financial was apparent in the comments of women asked whether they felt they were contributing to the war effort One said, "You've got something to work for now, besides your money, and that makes it more interesting and important" Another, less satisfied, said, "I'm conscientious about my job, but I can't understand the schedule and why we aren't allowed to make as much as we can" A third commented, "I thought we were helping at first, but with so much waiting for work, I don't think so now" The report makes it clear once more that the satisfied worker does better than the dissatisfied worker, and that the springs of human satisfaction are not purely materialistic

AN INTELLIGENCE CATALYST

THOUGH substances like amphetamine temporarily increase human intellectual efficiency, as judged by intelligence tests,[1] their psychic effects do not seem to have been worked out in animals Recently, however, data have accumulated about a substance which raises "intelligence" in rats, in the sense that it increases the level as well as the rate of learning. Surprisingly this substance is the amino-acid, glutamic acid, which besides being a common constituent of the diet is also synthesised by the body Albert and Warden[2] tested the intellectual performance of the rats by training them to overcome a series of obstacles in their search for food they had to step on a series of plates in a certain order before they could reach their food In the control group, 50% were able to learn a two-plate arrangement, and 25% a three plate arrangement Of the animals receiving glutamic acid, on the other hand, all were able to master two plates, nearly 90% could overcome a series of three plates, and one animal even learned the four- and the five-plate arrangement In another series of experiments Zimmerman and Ross[3] found that animals receiving 200 mg of glutamic acid daily could learn a maze three to four times as quickly as the controls Statistical analysis of the results showed them to be significant.

These results are not without a theoretical background Weil Malherbe[4] has shown that l glutamic acid is the only amino-acid which is directly metabolised by brain slices It has also been demonstrated[5] that glutamic and citric acids alone can reactivate dialysed choline acetylase, the enzyme which synthesises acetylcholine—which, of course, is intimately concerned with the transmission of nervous impulses Glutamic acid has also been used in the treatment of petit mal in children by Waelsch and his colleagues,[6] on the assumption that it would produce an acidosis which had previously been found beneficial in that condition As little as 5 g of l glutamic acid considerably reduced the number of fits in these patients, but this success could hardly be attributed to the extremely mild acidosis produced

Since glutamic acid occurs in the diet and milk is especially rich in it, the better scholastic achievement observed in school-children receiving extra milk may have an explanation so far unsuspected May the time never come when the letters FRS are merely an index of how much glutamic acid a man can put away

1 Sargant W Blackburn J M *Lancet* 1936 ii, 1385
2 Albert K F Warden C J *Science*, 1944 100, 476
3 Zimmerman F J Ross S *Arch Neurol Psychiat* 1944, 51, 416
4 Weil Malherbe H *Biochem J* 1936 30 665
5 Nachmansohn D, John H M, Waelsch, H *J biol Chem* 1943, 150 185
6 Price, J C, Waelsch H Putnam, T. J *J. Amer med Ass* 1943, 122 1153· Waelsch H., Price, J C *Arch Neurol Psychiat* 1944, 51 393

THE AFRICAN MEDICAL STUDENT

THE history of the coloured people in the United States has shown them to be responsive to education and not lacking in ability In South Africa, native people of the same stock are still backward, a prey to ignorance and disease The fault does not lie wholly with the legislators, they have had to contend with prejudice as profound and unreasoning as that which once shook the Southern States But there is evidence of growing liberality for example, a measure to provide old-age pensions for the African population, which could get no hearing ten years ago, has lately been passed

In the field of medicine the dark peoples of Africa have been at a special disadvantage. Their need for native-born doctors who will go into the villages and teach their own people can hardly be exaggerated, yet until the last few years there have been no facilities for training African medical students The idea of allowing an African to examine a white woman seemed, and still seems, unthinkable to the European population, and no medical school existed where students could acquire experience among members of their own race To send a young man to Great Britain to qualify is beyond the means of most African families one family succeeded, and Dr. R T. Bokwe, who qualified at Edinburgh some years ago, is now assistant district surgeon at Middledrift, Cape Province

In 1940 the University of Witwatersrand offered to provide a full course of medical and dental training for African students The government accepted the offer, and now give five scholarships yearly of £225 a year to enable students from the South African College at Fort Hare to take the course The first year is spent at Fort Hare, where the government offers bursaries for ten students yearly; from among these five are selected for scholarships At present 24 African students are taking the course, and the first three are expected to qualify this year They will be given house posts at the Victoria Hospital, Lovedale, the McCord Zulu Hospital at Durban, and elsewhere, and will later be offered suitable government posts among their own people The government has provided £33,500 to build a hostel for these students at the university; building was begun last November, and it is to be named the Douglas Smith Home, after the Secretary for Native Affairs whose keen interest in African education has done much to foster its advance

The numbers of students may seem small when set against the need, but now that the course has been founded it is likely to develop steadily It must be borne in mind that at present many Africans attending school do not pass beyond the third or fourth standard and more than half of them do not attend school at all The proportions of African children of school age who actually attend school are as follows 40% in Cape Province, 38% in Natal, 48% in Orange Free State, and 28% in the Transvaal The numbers who reach the equivalent of matriculation level are not high, and it will probably take advances in general education covering several years before the numbers of candidates suitable for medical training begin to approach the needs of the country. It is to be hoped that these advances will be made quickly as well as steadily, for the need is great and urgent Increasing interest in African education is shown by a rise in public expenditure on this item from £600,000 in 1936 to £2,632,000 in 1945

It should be added that other grades of African workers have long been trained for service among the villagers Thus at Fort Hare "medical aids" take a course lasting 4 years, mainly in preventive measures and practical sanitation, and finally sit for a degree in hygiene They are appointed to the health centres now being set up in native areas, holding posts under either the government or the local authorities African nurses are trained in large numbers at the mission and provincial hospitals, their courses being subsidised by the State They take the same nursing and midwifery qualifications as British nurses In the Transkei women social workers are trained in hygiene and mothercraft, and are taught something about the soil from the agricultural and nutritional points of view People of a simpler type are trained as health assistants; they undertake practical preventive wo[illegible] malarial mosqu[illegible]

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Blumgart, H L, Schlesinger M J Davis D Amer Heart J 1940 19 1

tion As Blumgart and his colleagues pointed out the development of a myocardial infarct depends largely on the duration of the period of anoxia If this period can be reduced, or if, while the blood supply to the affected area is reduced, the demands on the myocardium can be rapidly lowered by rest in bed, sedatives, or control of the rapid ventricular rate, then infarction may not occur Clinically such episodes may simulate myocardial infarction, but the typical electrocardiographic changes are not obtained and there is no pyrexia, leucocytosis, or raised sedimentation rate

THE PRACTITIONER AS TEACHER

SPEAKING as a medical officer of health Dr H R Tighe[1] argues that the general practitioner should not try to practise preventive medicine but should confine [illegible] eatment of disease Once [illegible], routine preventive work, [illegible] ver to the lay specialist or [illegible] he sanitary inspector, the [illegible] se the school teacher, the [illegible] liceman the social welfare [illegible], and recently the officials [illegible] ong the host of lay workers

"if the general medical [illegible] g to gain honour or glory [illegible] g with these experts he is [illegible] those who say that the [illegible] perpetually preaching the [illegible] declares that mere talk, [illegible] thing to persuade "the [illegible] ler control, the dull not to [illegible] to have children or the [illegible] children" and it will do [illegible] ctivities of the avaricious [illegible] ms or the adulterator of [illegible] that talk is sometimes [illegible] octor the right person to [illegible] nnda?

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[1] Publ. Hlth January 1945 p 43

Annotations

The amino-acid 'glutamic acid' — common constituent of diet also synthesized by body.

Raises intelligence in rats i.e. inc^s. the level & rate of learning — Found by —

I Albert & Warden — by training them to overcome series of obstacles in search of food

Control — glutamic a

50% - peanut 2-plate — all

arrgnut.

25% - 3-plate. — 90%

4½-Plate ← one rat

II. Ross & Zimmerman — animals getting 200 mg. glutamic a. daily peanut a maize 3, 4 times earlier than controls

day-rates, group piece-rates, and individual piece-rates Women working on individual piece-rates were the best paid but the least satisfied with the wage system, because of inequalities in rates or amounts of payment between different individuals Much more popular, though the wages were less, was the group piece-rate system, which appealed to the social qualities of coöperation, tolerance, and mutual help But by far the most popular system was the day-rate, although it was the worst paid several women referred to the higher quality of work possible under this system where the speed of work is not the primary consideration It is interesting that 75% of women preferred day work to night work, despite its lower rates of pay The value of an incentive beyond the financial was apparent in the comments of women asked whether they felt they were contributing to the war effort One said, "You've got something to work for now, besides your money, and that makes it more interesting and important" Another, less satisfied, said, "I'm conscientious about my job, but I can't understand the schedule and why we aren't allowed to make as much as we can" A third commented, "I thought we were helping at first, but with so much waiting for work, I don't think so now" The report makes it clear once more that the satisfied worker does better than the dissatisfied worker, and that the springs of human satisfaction are not purely materialistic

AN INTELLIGENCE CATALYST

THOUGH substances like amphetamine temporarily increase human intellectual efficiency, as judged by intelligence tests,[1] their psychic effects do not seem to have been worked out in animals Recently, however, data have accumulated about a substance which raises "intelligence" in rats, in the sense that it increases the level as well as the rate of learning Surprisingly this substance is the amino-acid, glutamic acid, which besides being a common constituent of the diet is also synthesised by the body Albert and Warden[2] tested the intellectual performance of the rats by training them to overcome a series of obstacles in their search for food they had to step on a series of plates in a certain order before they could reach their food In the control group, 50% were able to learn a two plate arrangement, and 25% a three-plate arrangement Of the animals receiving glutamic acid, on the other hand, all were able to master two plates, nearly 90% could overcome a series of three plates, and one animal even learned the four- and the five-plate arrangement In another series of experiments Zimmerman and Ross[3] found that animals receiving 200 mg of glutamic acid daily could learn a maze three to four times as quickly as the controls. Statistical analysis of the results showed them to be significant

These results are not without a theoretical background. Weil-Malherbe[4] has shown that l-glutamic acid is the only amino-acid which is directly metabolised by brain slices It has also been demonstrated[5] that glutamic and citric acids alone can reactivate dialysed choline acetylase, the enzyme which synthesises acetylcholine—which, of course, is intimately concerned with the transmission of nervous impulses Glutamic acid has also been used in the treatment of petit mal in children by Waelsch and his colleagues,[6] on the assumption that it would produce an acidosis which had previously been found beneficial in that condition As little as 5 g of l-glutamic acid considerably reduced the number of fits in these patients, but this success could hardly be attributed to the extremely mild acidosis produced.

Since glutamic acid occurs in the diet and milk is especially rich in it, the better scholastic achievement observed in school-children receiving extra milk may have an explanation so far unsuspected May the time never come when the letters FRS are merely an index of how much glutamic acid a man can put away

1 Sargant W, Blackburn J M *Lancet* 1936 II, 1385
2 Albert K F Warden C J *Science* 1944, 100, 476
3 Zimmerman F J, Ross S *Arch Neurol Psychiat* 1944, 51, 446
4 Weil Malherbe, H *Biochem J* 1936 30 665
5 Nachmansohn D, John H M, Waelsch, H *J biol Chem* 1943, 150 485
6 Price J C Waelsch H Putnam, T J *J Amer med Ass* 1943 122 1173 Waelsch, H. Price, J C *Arch Neurol Psychiat* 1944, 51, 393

THE AFRICAN MEDICAL STUDENT

THE history of the coloured people in the United States has shown them to be responsive to education and not lacking in ability In South Africa, native people of the same stock are still backward, a prey to ignorance and disease The fault does not lie wholly with the legislators, they have had to contend with prejudice as profound and unreasoning as that which once shook the Southern States But there is evidence of growing liberality for example, a measure to provide old-age pensions for the African population, which could get no hearing ten years ago, has lately been passed

In the field of medicine the dark peoples of Africa have been at a special disadvantage Their need for native born doctors who will go into the villages and teach their own people can hardly be exaggerated, yet until the last few years there have been no facilities for training African medical students The idea of allowing an African to examine a white woman seemed, and still seems, unthinkable to the European population; and no medical school existed where students could acquire experience among members of their own race. To send a young man to Great Britain to qualify is beyond the means of most African families one family succeeded, and Dr R T Bokwe, who qualified at Edinburgh some years ago, is now assistant district surgeon at Middledrift, Cape Province

In 1940 the University of Witwatersrand offered to provide a full course of medical and dental training for African students The government accepted the offer and now give five scholarships yearly of £225 a year to enable students from the South African College at Fort Hare to take the course The first year is spent at Fort Hare, where the government offers bursaries for ten students yearly, from among these five are selected for scholarships At present 24 African students are taking the course, and the first three are expected to qualify this year They will be given house posts at the Victoria Hospital, Lovedale, the McCord Zulu Hospital at Durban, and elsewhere, and will later be offered suitable government posts among their own people The government has provided £33,500 to build a hostel for these students at the university, building was begun last November, and it is to be named the Douglas Smith Home, after the Secretary for Native Affairs whose keen interest in African education has done much to foster its advance

The numbers of students may seem small when set against the need, but now that the course has been founded it is likely to develop steadily. It must be borne in mind that at present many Africans attending school do not pass beyond the third or fourth standard and more than half of them do not attend school at all The proportions of African children of school age who actually attend school are as follows 40% in Cape Province, 38% in Natal, 48% in Orange Free State and 28% in the Transvaal The numbers who reach the equivalent of matriculation level are not high, and it will probably take advances in general education covering several years before the numbers of candidates suitable for medical training begin to approach the needs of the country. It is to be hoped that these advances will be made quickly as well as steadily, for the need is great and urgent Increasing interest in African education is shown by a rise in public expenditure on this item from £600,000 in 1936 to £2,632,000 in 1945

It should be added that other grades of African workers have long been trained for service among the villagers Thus at Fort Hare "medical aids" take a course lasting 4 years, mainly in preventive measures and practical sanitation, and finally sit for a degree in hygiene They are appointed to the health centres now being set up in native areas, holding posts under either the government or the local authorities African nurses are trained in large numbers at the mission and provincial hospitals, their courses being subsidised by the State They take the same nursing and midwifery qualifications as British nurses In the Transkei women social workers are trained in hygiene and mothercraft, and are taught something about the soil from the agricultural and nutritional points of view People of a simpler type are trained as health assistants; they undertake practical preventive work—for example, spraying to destroy malarial mosquitoes

Medical services to Africans have hitherto been given largely by missionary hospitals assisted by public grants The present government programme is largely the outcome of the Health Commission's report of 1944, it is wider than any previous one, and likely to grow

CLARIFYING CORONARY DISEASE

THE rising incidence of circulatory diseases and the increasing proportion of old people in the population demand a clarification of our ideas concerning the diagnosis, treatment, and prognosis of disease of the coronary system. Our knowledge of the subject has advanced a long way since Herrick first showed that coronary thrombosis can be diagnosed at the bedside, but it has proved difficult to correlate satisfactorily the clinical, pathological, and electrocardiographic findings The necropsy study by Blumgart and his colleagues[1] of 125 consecutive cases in which the coronary arteries were injected post mortem threw much fresh light on the problem In normal hearts anastomotic communications less than 40 micra in diameter exist between the coronary arteries, but these are probably of little value in overcoming the untoward effects of sudden coronary occlusion Intercoronary anastomoses greater than 40 micra do not exist in normal hearts they are found in the presence of coronary sclerosis, but only when and where required No evidence was found that such anastomoses increase with age in the absence of arterial narrowing This anastomotic development explains many of the apparent anomalies Thus, if coronary occlusion develops slowly, it may result in the complete occlusion of at least one of the major coronary arteries without there being more than a moderate degree of myocardial fibrosis, in such cases the collateral circulation develops pari passu with the occlusion, so that the blood supply to the myocardium in the affected area is adequate for its local requirements though if the demands on it increase the patient will show the typical clinical picture of angina pectoris. On the other hand, if the occlusion develops more rapidly than the anastomosis the myocardium will show varying degrees of fibrosis.

In other words, coronary thrombosis (or occlusion) does not produce any characteristic clinical manifestation The condition commonly referred to under this label by clinicians, and characterised by severe substernal pain, shock, hypotension tachycardia, pyrexia, leucocytosis, and typical electrocardiographic changes is due to myocardial infarction and only incidentally to coronary thrombosis. For this reason it would be well to use the term myocardial infarction instead of coronary thrombosis This was the practice among clinicians twenty years ago, and it is not clear why the name was ever given up If it is reinstated we shall be able to refer to coronary occlusion which is either chronic, resulting in angina pectoris or acute, resulting in myocardial infarction As Blumgart and his colleagues pointed out the development of a myocardial infarct depends largely on the duration of the period of anoxia If this period can be reduced or if, while the blood supply to the affected area is reduced, the demands on the myocardium can be rapidly lowered by rest in bed, sedatives, or control of the rapid ventricular rate, then infarction may not occur Clinically such episodes may simulate myocardial infarction, but the typical electrocardiographic changes are not obtained and there is no pyrexia, leucocytosis or raised sedimentation rate

1 Blumgart, H L Schleisinger M J Davis D *Amer Heart J* 1940 19 1

THE PRACTITIONER AS TEACHER

SPEAKING as a medical officer of health, Dr H R Tighe[1] argues that the general practitioner should not try to practise preventive medicine but should confine himself to the diagnosis and treatment of disease Once the stage of pioneering is past, routine preventive work, he says is generally handed over to the lay specialist or to the lay public. Today "the sanitary inspector the health visitor, the school nurse, the school teacher, the engineer the architect, the policeman the social welfare officer the newspaper reporter, and recently the officials of the Ministry of Food, are among the host of lay workers in preventive medicine,' and 'if the general medical practitioner thinks he is going to gain honour or glory, much less riches, by competing with these experts, he is greatly mistaken' Against those who say that the doctor must be a teacher, perpetually preaching the gospel of health Dr Tighe declares that mere talk, without coercion will do nothing to persuade "the mental defective to remain under control, the dull not to multiply, the physically fit to have children, or the physically unfit not to have children," and it will do equally little to combat the activities of the avaricious industrialist, the owner of slums or the adulterator of food And even assuming that talk is sometimes effective is the individual doctor the right person to undertake this form of propaganda?

> I cannot imagine he is or that he really desires the office I cannot imagine that the general medical practitioner desires to turn himself into a living gramophone record to keep repeating what to him must be the same platitudes ad nauseam If there be any who consider this to be suitable work for the product of the most lengthy and expensive professional training known I cannot share their view I should regard the school teacher the health visitor the public lecturer, the newspaper the cinema, the billposter and the wireless as the proper media I do not deny that the doctor should play an important part in all such health education but his work should be collective not individual.'

Dr Tighe's thesis is, in fact, that two main divisions of medicine should be recognised and maintained. First there is clinical medicine, concerned in the widest sense with diagnosis and treatment, and secondly there is preventive medicine, concerned with the prevention of disease or injury, the maintenance and improvement of health, and the improvement of the race both mentally and physically The practitioner of clinical medicine should know how and when to link up with the organisation of preventive medicine but his essential job should be to discover disease and to treat it, not to keep people well or to prevent disease" The practitioner of preventive medicine on the other hand should concentrate his thoughts "not only on prevention as distinct from cure but on the human herd as distinct from the individual, for to him the individual is of small account'

Obviously this argument runs counter to a great deal that is nowadays being said and thought about the general practitioner's functions; and it may appeal to many practitioners who cannot quite see themselves in the rôle cast for them by some of the exponents of 'positive health But even those who agree that clinicians must always be mainly interested in diagnosis

1 *Pub. Hlth* January 1945 p. 43.

and treatment may hesitate to go so far as Dr Tighe in excluding them from preventive work Surely he over-simplifies when he accepts the definition that "preventive medicine is that which starts off with health and sees to its maintenance, and clinical or curative medicine is that which starts off with disease and endeavours to effect its cure or amelioration"? Health and disease cannot be such definite entities as this implies they are better conceived as different ends of a scale which records the degree of success in reacting to environment Perhaps therefore the clinician need not trouble to pursue, with Dr Tighe, such academic questions as whether prevention does or does not embrace treatment of the small beginnings of disease, or the avoidance of sequelæ His task is simply to give the help and advice most likely to be useful to his patient, regardless of whether this advice can be labelled curative or preventive

Any new boundary between the territories of the medical officer of health and the practitioner can hardly give the whole field of preventive medicine to the former. In so far as they must be separated, the natural division appears to lie between communal medicine on the one hand and personal medicine on the other The clinician is concerned primarily with the individual, while the MOH is concerned primarily with the community , But preventive medicine can properly be practised by both.

A SERVICE FOR DOCTORS AND PATIENTS

THE problem of disposing of patients in need of immediate hospital treatment has exercised both town and country doctors for many years In 1938 King Edward's Hospital Fund for London determined to make an attempt to solve the problem for the London area by initiating, after discussions with the Voluntary Hospitals Committee, the Voluntary Hospitals Emergency Bed Service This service opened in June, 1938, and in its first year dealt with 7859 cases The rapid increase in the number of calls in the first half of 1939, when 5131 cases were dealt with, showed that the service was valued At the outbreak of war the work was interrupted for three weeks, when the whole staff was lent to the Ministry of Health to help in the organisation of the Emergency Medical Service It was then opened again and records of the period between 1940 and the end of the flying-bomb attacks show that calls on it increased rapidly whenever conditions in London became relatively normal Cases dealt with in the first half of 1945 have been more numerous than in any other half-year since July, 1940 It seems that as soon as the London population becomes stable and hospitals extend their activities to pre-war limits, the scope of the service is bound to increase

It operates on a system now backed by seven years' experience, and has reached a high pitch of efficiency Doctors who in the past have waited, weary and exasperated, by a telephone at their own or at a patient's house, will be surprised to know that the average number of telephone calls to hospitals for each admission through the Emergency Bed Service has never exceeded 1 7 in any one year, and has at times been as low as 1 5 The flexibility of the arrangements is well illustrated by an incident of the flying-bomb period when the building which housed the EBS was damaged by a flying bomb two minutes after a call came through The staff on duty, despite minor injuries, moved down to the emergency telephone in the basement, booked a bed at a hospital, arranged for the ambulance to collect the patient and rang the doctor back to say that all arrangements had been made within 20 minutes of receiving the call Happily the service may now look forward to emergencies of a more peaceable nature, of which it already has some experience Its records show that on one occasion it succeeded within 10 minutes in tracing a doctor's aunt who lived alone in London, and had disappeared without trace, after being taken acutely ill

Owing to the nature of its work the EBS has a comprehensive view of the hospital needs of the metropolitan area It has constant evidence of the acute shortage of accommodation for chronically sick and aged people who though not presenting acute emergencies need either hospital treatment or institutional care. Waiting lists offer complex problems the patient must be allowed to choose the neighbourhood in which he wants to be treated and the doctor under whom he is to be admitted; and the hospital which has advised treatment through its expert medical staff must be responsible for carrying that treatment through to a conclusion The problems are greater in magnitude than those already solved, but not different in kind, and having gained the confidence of doctors and hospital authorities the EBS may well help to overcome another of their joint difficulties

It is important that London doctors should know what the service has to offer at the present time; besides being able to arrange for the admission of patients to hospital with the least possible delay, it provides ambulance when necessary, and informs the doctor by telephone when arrangements are complete. The is always asked if he prefers any particular hospital, he often leaves the choice open. Before the war, the service used to work all night it now operates from 9 to 10 PM daily, and hopes to resume all-night when the labour position becomes easier. In the telephone book, it is given under the heading of Emergency Bed Service, the numbers being City 2162 and Clerkenwell 6571.

EWART'S SIGN

WHEN William Ewart,[1] then physician to St. George's Hospital, published his classical paper on pericardial effusion nearly fifty years ago he described ten diagnostic signs, the eighth (the posterior pericardial patch of dullness) and the tenth (the posterior pericardial patch of tubular breathing and ægophony) of which together came to be known as Ewart's sign These findings were for long accepted as among the classical signs of pericardial effusion, being ascribed to pulmonary collapse as a result of pressure on the bronchi by the distended pericardium, although it has also been suggested that Ewart's sign only occurs in rheumatic cases where it is due to rheumatic pneumonia Incidentally, Ewart's sign is not mentioned in Morton's revised edition of Garrison's *Medical Bibliography*, while one well-known English textbook refers to it as Bamberger's sign The specificity of the sign has gradually come under suspicion, similar findings having been described in patients with a large left auricle in whom there was no evidence of a pericardial effusion American workers[2] have now suggested that all types of cardiac enlargement may produce one or more of the following signs over the lower lobe of the left lung an area of dullness just below the angle of the left scapula, sometimes only elicited on heavy percussion, a prolongation of the expiratory breath-sound varying from that in bronchovesicular breathing to that obtained in bronchial breathing; diminished breath-sounds, crepitations, and an increased, almost nasal, vocal resonance In none of the patients on whom the American study was based was there any evidence of other conditions, such as pulmonary infarction, congestion, an elevated diaphragm or pericardial effusion, that might account for these signs The findings are said to be most common with an enlarged left auricle, as in mitral stenosis, and it should be remembered that in hypertension the left auricle is often considerably enlarged and may be displaced backwards by the hypertrophied left ventricle

1 Ewart, W *Brit med J* 1896 1, 717
2 Chapman, E M, Sanderson, R G *Ann intern Med* 1945, 23, 3
3 Babey, A *Amer Heart J* 1937, 13, 228

Special Articles

THE MEDICAL OFFICER AS PRISONER IN GERMANY

A L. COCHRANE, M B CAMB
CAPTAIN RAMC

THE fact of being taken prisoner undoubtedly enhanced the importance of all working MOs relative to that of other officer prisoners-of war There were several reasons for this : they were the only officers, except a few dentists, padres, and interpreters, who remained in contact with the other ranks , they were the main group of officers in contact with Allied prisoners , and, being surrounded by the rather nebulous halo of " protected personnel," they were in a better position than other POWs to approach, argue with, and possibly get something out of the Germans They were, too one of the luckiest occupational groups among officer POWs In company with the poets, artists, musicians, dentists, and padres they could go on doing their ordinary job As " protected personnel " the working MOs had slightly better living accommodation, and could write more letters and go for more walks

On the other hand they had to pay heavily for their privileges. The MOs, particularly those working in the international hospitals, were faced with unexpected difficulties, loaded with odd responsibilities, and forced to take decisions on matters of general importance in relative isolation

Hospitals inevitably became much more than hospitals they became information bureaux, centres for complaints, secret post-offices, headquarters for security, news centres, and holiday camps They were the meeting-places of many different nations, with all the attendant possibilities of comradeship or friction and in each of these varied functions the MO became inevitably involved

In all this sort of work there was a crying need for a few general principles on which to base his day to-day decisions, but unfortunately the essential duality of the MO s position in any army becomes accentuated in captivity, when the good health of the troops becomes an advantage to the detaining power for whom he works It seemed sometimes as though there were two distinct and incompatible ideals of behaviour for the MO As an officer he should refuse to do anything which helped the enemy's war effort. Logically this meant that he could only treat officers and NCOs who did not work for the enemy, and chronic diseases among the other ranks, in which recovery was unlikely in Germany It could be argued that, if British MOs refused to treat the POW workers of all nationalities the Germans would have to do it, and the German medical service would be strained to breaking point The other ideal was that rather suggested by the Geneva Convention, which visualises an MO who is not a prisoner who confines his attention entirely to medicine, collaborating with the enemy MOs and is rapidly repatriated Pure types of either " ideal " were non-existent ; the British being British, compromised, but the proportion of the two ideals in the final compromise varied considerably By a judicious mixing of the two ideals it was possible to justify most lines of conduct MOs were isolated, and there were few, if any, directives ; so in general each went his own sweet way, producing a regrettably variable standard throughout Germany

MEDICAL WORK AND ITS DIFFICULTIES

The most striking thing about the medical work was its continuity and quantity Many MOs worked for 4 or 5 years with very little time off. I did 4 years, with no medical work on 22 days, some of which were spent in travelling The medical cases, as I saw them, consisted chiefly of tuberculosis and psychoneurosis, with deficiency diseases, chiefly hypoproteinaemia and beriberi, during the first and last 6 months, with some typhus in the middle

The chief difficulty that faced MOs was naturally their lack of training in treating tuberculosis and psychoneurotics Imprisonment exposed a very serious gap in British medical education, and many POWs suffered as a result Besides, diets for tuberculous patients were particularly hard to arrange The British POWs did fairly well with Red Cross parcels, but a British MO in charge of tuberculous Russians, French, or Serbians had difficulty in deciding how much food to divert from the British to the Allies Later an excellent international hospital for tuberculous POWs was organised at Elsterhorst, where treatment compared favourably with many British war time sanatoria Its excellence was, however, a tribute to the Red Cross and not to the Germans

As regards the psychoneurotics, it was difficult enough to treat them in English, but facing them in a foreign tongue produced a feeling of complete helplessness I like to think I cured some Serbian hysterics, but they probably relapsed We were, however, owing to the overlap in symptomatology, kept very busy excluding tuberculosis amongst these neurotics The incidence of tuberculosis was very high, running to 0% per annum among Russians, diagnosed clinically and confirmed radiologically

The work was complicated in many other medical or extramedical ways. We were, for instance, constantly short of drugs, and improvisation was difficult I had to treat, or rather keep alive, a diabetic with acetonuria without insulin for 6 weeks X ray films were always scarce, and too many diagnoses had to be based on screening Electrocardiograms and blood sugar curves were in some areas unobtainable, and at Salonika diphtheria serum was limited to 6000 units per case

The hospitals suffered through the absence of nurses, and we were often short of orderlies For 120 medical beds, including 20–30 for tuberculosis, we had only 8 orderlies, who had to fetch food, do day and night duty, and run the laboratory

The languages were another wicked complication, which made diagnoses difficult, lengthened the work, and ruined one's temper At one period I had to talk six languages every day to get through the work ; at another I had to take histories in Serbian and write them in German—and this was in no way exceptional. Very many doctors, like myself, treated many more French, Russian, and Serbian patients than they treated British In all, I treated patients from about 30 different countries

The internal discipline of the hospital was another headache Theoretically a POW MO could enforce his authority through the Germans, but he was ill advised to try it except in very exceptional cases as it usually led to a total loss of authority One rapidly learnt never to give an order unless one knew it would be obeyed This meant more discussion and explanation with the staff about general policy, and was probably all to the good, though at times very irksome The difficulties were again increased by having orderlies of various nationalities. At Wittenberg there were British, Russian, French, Italian, and Dutch in a staff of 91 There were occasionally ugly moments when a " browned off " orderly or patient refused to obey an order, and there was little you could do about it if he was bigger than you were But on the whole the loyalty of the orderlies in very trying circumstances was extraordinary, and all of them—Russian, French, Serbian, Italian, Dutch, NZMC, AMC, FAU, and RAMC—deserve great credit The best orderly I ever had was a Russian, Ivan.

INTERNATIONAL COMPLICATIONS

The international mixture in the wards led to further complications. The Allied POWs were subjected to intense propaganda from the Germans and it was clearly up to the doctors, who were practically the only British officers in contact with the Allies to do something about it Each country presented its own particular problems The French wanted to know why we sank their fleet, why the German ships got up the Channel, why some bombing of France was none too accurate, who de Gaulle was, and whether we were going to take Syria The Serbs wanted to know who Tito was and why Mikailovich fought him, and the Poles wanted to know about Katyn. The Russians asked about the invasion after the last war, about Munich, and later about Greece, and they all wanted to know when the Second Front was coming It was, as can be imagined, a difficult job To do it well one needed to be a polyglot, a historian a statesman, and a prophet and doctors in general are none of these things ; but we tried and did something to break down that wall of suspicion separating us from Europe

Another minor problem was knowing which types of people one should not treat. French POWs working in

munition factories, "liberated" French POWs, Russians working in German AA, all presented difficulties

The international POW situation was further complicated by the economic strata which inevitably appeared Our weekly parcels saved our lives but ruined our reputations; the British became the "bloated capitalists" of POW life We had about 3000 calories a day in hospital, while the Russians would only have the 1600 calories from the Germans The Serbs and French, who got some parcels, were in an intermediate position When such groups were mixed in one ward they had to share or fight, and, as the British were on the whole averse to sharing, although they were often charitable, friction was inevitable It was unfortunate that it was impossible to send sufficient parcels to give all the patients in these mixed hospitals a parcel a week The propaganda effect would have been very great, as it was, the MOs had to labour to make propaganda and keep the peace against this economic impasse

RELATIONS WITH THE GERMANS

There was also plenty of extramedical work in connexion with the British POWs News had to be organised and difficulties arranged, medical orderlies had to get their recognition papers, and NCOs who were voluntarily working for the Germans had to be weeded out A great deal of this was done at Stalag, but some always came to the MO

Repatriation raised another host of problems How to discourage hopeless cases from going up to the commission, so that the genuine cases should not suffer? How to present doubtful cases? How to convince the "board" that a man was psychoneurotic? Feeling ran so high at "board-time" that a false move might cause a lot of trouble It was unfortunate that London or Geneva did not bring some pressure to bear on Germany to organise the repatriation of orderlies. Many orderlies who had been captured in France waited to the end, whereas many captured in Greece and later, were repatriated earlier

Externally our difficulties were the Germans, and from the MO's point of view the chief one was the German MO. Naturally we got the worst MOs in Germany They were, in general, uninterested in medicine and concentrated their energies on getting POWs out of hospital as soon as possible There were others who were better, but I never seemed to meet them

With the usual type the technique was roughly as follows The first problem was to convince the German MO that you were a better doctor than he was If you spoke German, this could be done fairly quickly. This was followed by a concentrated attack on him to give the serious cases a fair deal During this period "holidays" and malingering had to be discouraged He usually capitulated after a few months, and then you could go slowly ahead arranging holidays for the tired POWs, keeping psychoneurotics in hospital under another diagnosis, and organising malingering It was not easy, for pathological findings were often controlled, and one had to rely on the patients' dramatic powers and one's own power of bluff in German

It was amazing how effective the malingering was In the Wittenberg area in the winter 1944–45, on an average 25% of 1000 French POWs were off sick every day There were also 20% of the Russians off, and about half the Russians and three-quarters of the French were malingerers The British never rose above 10%, they looked too healthy and were poor actors There was a German sergeant always on the sick-parades, and, if he thought I was pulling a fast one, the case was sent to a German doctor If the malingering was discovered, I was in danger of sabotage trial, so I could only use good actors As it is possible that other MOs may suffer from my teachings, I wish to warn them against atypical hæmaturias, even when the urine is passed in their presence, and atypical bilateral parotitis

Relations with German other ranks were easier Most of them had their price in cigarettes or chocolate This proved of great value not only in security work but also in deals on the black market At the tuberculosis hospital at Elsterhorst a large organisation was built up, involving most of the German staff, whereby we bought extra food on the black market, which made a great difference to the patients' diet It was, however, difficult, tedious and rather disgusting work.

The dangers to which POWs were exposed were re without being exceptional Many of those captured Crete and Greece may claim to rank among the mo experienced "bombees," as they had gone through th blitz in England and Crete, followed by the Angl American blitz in Germany, in which many POW including MOs and orderlies, died (These raids pr duced an exquisite example of conscious ambivalence Some, like myself, ended their front-line experience wi 5 days under Russian artillery fire

In the early days of captivity the Germans were n above firing at the hospitals inside the cage in broa daylight—apparently out of sheer exuberance Thre orderlies were wounded in this way at Salonika in 1941 two died, and one lost his arm. On the next day the scored a near miss on myself during my morning round

The typhus epidemic of 1941–42 in Germany took it toll of POW medical personnel At least 2 doctors die and several orderlies, and of the 5 RAMC officers wh treated tuberculous patients for any length of time, on I am told, developed tuberculosis

A BALANCE-SHEET—AND SOME SUGGESTIONS

In conclusion it may be said that the POW MO laboured hard and long medically and extramedicall under very difficult conditions In comparison wi other POW officers they were lucky, in comparison wi their non-POW colleagues they were very unluck They lost all chance of promotion medically or militarily they ran a definite risk of permanent psychologic trouble; they lost a vast amount of leave They ca only congratulate themselves on having missed a va amount of paper work!

As there will possibly be other wars, it seems reasonab to make some suggestions The first would be that th RAMC should keep in touch a little more with POW MOs Instructions could be sent secretly, or medic literature, cigarettes, or even best wishes could be sen openly (after all, the BMA did it) This would hav reduced our feeling of isolation and led to a more unifie approach to our problems

The second would be that leave on liberation shoul vary with time of imprisonment Six weeks after 4 or years in the bag is extraordinarily short, if the POW ha been working all the time How many days off did a non-POW MO have in the same period?

Then finally a little more care might be taken in placing liberated MOs on their return At the beginning of th war I bore the "bump" of the change from medic research to being MO to a Middle East Command (Lay Force) fairly well One expected a certain amoun of confusion then. But the "bump" back from being a physician, treating mostly tuberculous patients, for years in six languages to being the dog's body of a gener hospital is much more difficult for a tender POW "psyche" to cope with. Perhaps it will be better next time

THE MINISTER'S SPEECH TO MEDICAL OFFICERS OF HEALTH

Mr ANEURIN BEVAN, Minister of Health, speaking at the annual luncheon of the Society of Medical Officers of Health in London on Sept 21, said he would have regretted the severance of housing from the other responsibilities of his Ministry at this juncture Except perhaps nutrition nothing was more important to health than housing It was a pity that housing was always tackled in circumstances of emergency, but it was his duty not to surrender to temporary situations, and he intended to see that the houses built after this war by local authorities were more spacious than some of those built after the last one What had to be done was to bring down the cost of building he did not subscribe to the traditional view that because a commodity is scarce its price must therefore be high—a belief disproved during the war Housing should not be left to the law of supply and demand, but should be organised on a scientific programme Nothing contributed more to the neurosis of modern society than the inability of young people when they got married, to shut the door behind them and enjoy privacy in their own home This winter would be a situation when young men and women coming out of the Services and marrying would be obliged to share houses with other people That situation must be faced but also it must be done away with as soon as possible

Turning to the prevention of tuberculosis, Mr Bevan described it as a national disgrace that soldiers coming to this country from the United States should be forbidden to drink the milk our children drink He intended to give this matter urgent consideration and he hoped for the support of the medical profession

The shortage of nurses, he continued, was approaching the dimensions of a national disaster One explanation for it might be that nurses are expected to do too much domestic work. "We must also realise that it's time we got some way away from the Florence Nightingale tradition" Nursing as a vocation must be combined with a reasonable standard of livelihood Some progress had been made through the Rushcliffe report but more was needed A great campaign would be started shortly to attract recruits to nursing He hoped that the hospital services would find a place for demobilised male orderlies.

In conclusion the Minister said that, faced with the possibility this winter of epidemics such as followed the last war, he was doing all he could to ensure the speedy release of doctors from the Forces As for the future, nothing could be dearer to his heart than the establishment of a health service in this country that would be the envy of the world

Prof R M F PICKEN, the president replying to Mr Bevan's toast of the Society said that the success of a National Health Service will depend on the quality of the men and women engaged in it it will not succeed unless it attracts the best brains. Those designing the new organisation would, he felt, do well to study the attitude of mind of doctors in the public health service towards their own service They should examine its attractions and repulsions, and consider why in recent years it had not been receiving quite its share of the best brains in the medical profession The reasons would be worth analysing before launching into something bigger Professor Picken assured the Minister that the whole profession would be behind him in his effort to clean up milk.

MEDICAL DEFENCE UNION

AT the first peace-time annual meeting since 1938, Dr JAMES FENTON, the president, spoke of war-time experiences, and plans for the future The council and its committees met in London throughout the war, and the office staff, after trying exile in the suburbs, came back to Bedford Square in 1942 Membership has risen from 126 in the first year (now nearly 60 years ago) to 28 483 today; and some 8000 members have been added since 1938 Both litigation and the cost of defence have, it seems, increased during the war Demobilised doctors face special problems, and many of them have already been advised by the Union Dr Fenton urged members to consult it as early as possible when they are threatened with litigation: cases are prejudiced by delay, and often by action taken without advice He also reminded them that they fall out of benefit if they fail to pay their subscriptions.

During the past year the Union has held discussions with the London and Counties Medical Protection Society and with the Scottish Defence Union, with a view to establishing a joint coördinating committee The main object of this committee, Dr Fenton said, will be to define the broad policy to be pursued by the three societies in common; and advantage may be expected from joint action in cases affecting members of two or more societies

Discussions are also being carried on with the Society of Anæsthetists and with manufacturers of anæsthetic gases in an attempt to prevent accidents due to the use of wrong gas-cylinders This is difficult to achieve, because new forms of coupling have to be tried and manufactured, and plans for the special colouring of cylinders will take some time to fulfil, since they affect not only Great Britain but America, Australia France, and Germany A short term plan is being followed for the time being and a long term policy designed to make the apparatus foolproof will be adopted as soon as possible

Mr St J D BUXTON was unanimously elected president, Dr HENRY ROBINSON treasurer and Dr G ROCHE BERCH chairman of the council committee The retiring president and treasurer (Dr Fenton and Mr F D D DAVIES) received the thanks of the meeting, for their work in the difficult circumstances of war

In England Now

A Running Commentary by Peripatetic Correspondents

MY peripatetic colleague's reflections last week on the atomic bomb bring to mind the late Wilfred Trotter's remarks on (to all intents and purposes) the same subject They arose from his observations on the different ways in which different people resolve the everlasting conflict between herd suggestion and their own experience

The solutions by indifference by rationalisation or by a mixture of these two processes (he wrote) are characteristic of the great class of normal sensible reliable middle age *with its definite views, its resiliency to the depressing* influence of facts and its gift for forming the backbone of the State In them herd suggestion shows its capacity to triumph over experience to delay the evolution of altruism and to obscure the existence and falsify the results of the contest between personal and social desires. That it is able to do so has the advantage of establishing existing society with great firmness but it has also the consequence of entrusting the conduct of the State and the attitude of it towards life to a class which their very stability shows to possess a certain relative incapacity to take experience seriously, a certain relative insensibility to the value of feeling and to suffering and a decided preference for herd tradition over all other sources of conduct

Amongst the *first-class Powers* today the mentally stable are still the directing class and their characteristic tone is discernible in national attitudes towards experience, in national ideals and religions, and in national morality It is thus possession of the power of directing national opinion by a class which is in essence relatively insensitive towards new combinations of experience, this persistence of *a mental type which may have been adequate in the simpler* past, into a world where environments are daily becoming more complex—it is this survival so to say of the waggoner upon the footplate of the express engine which has made the modern history of nations a series of such breathless adventures and hairbreadth escapes To those who are able to view national affairs from an objective standpoint, it is *obvious that each of these escapes might very easily have* been a disaster, and that sooner or later one of them must be such

Later in his great book he presents the same argument again:

The actual mechanism by which society, while it has grown in strength and complexity has also grown in confusion and disorder is that peculiarity of the gregarious mind which automatically brings into the monopoly of power the mental type which I have called the stable and common opinion calls normal This type supplies our most trusted politicians and officials, our bishops and headmasters our successful lawyers and doctors and all their trusty deputies assistants, retainers, and faithful servants *Mental stability is their leading characteristic, they* "know where they stand" as we say they have a confidence in the reality of their aims and their position an insensibility to new and strange phenomena a belief in the established and customary, a capacity for ignoring what they regard as the unpleasant the undesirable, and the improper and a conviction that on the whole a sound moral order is perceptible in the universe and *manifested in the progress of* civilisation

Civilisation through all its secular development under their rule has never acquired an organic unity of structure; its defects have received no rational treatment but have been concealed ignored and denied instead of being drastically rebuilt it has been kept presentable by patches and buttresses by paint and putty and whitewash The building was already insecure and now the storm has burst upon it, threatens incontinently to collapse

The war was the consequence of inherent defects in the evolution of civilised life it was the consequence of human progress being left to chance and to the interaction of the heterogeneous influences which necessarily arise within a gregarious unit whose individual members have a large power of varied reaction In such an atmosphere minds essentially resistive alone can flourish and attain to power and they are by their very qualities incapable of grasping the necessities of government or translating them into action.

The method of leaving the development of society to the confused welter of forces which prevail within it is now at last reduced to absurdity by the unmistakable teaching of

events, and the conscious direction of man's destiny is plainly indicated by Nature as the only mechanism by which the social life of so complex an animal can be guaranteed against disaster and brought to yield its full possibilities

A gregarious unit informed by conscious direction represents a biological mechanism of a wholly new type, a stage of advance in the evolutionary process capable of consolidating the supremacy of man and carrying to its full extent the development of his social instincts

Such a directing intelligence or group of intelligences would take into account before all things the biological character of man, would understand that his condition is necessarily progressive along the lines of his natural endowments or downward to destruction It would abandon the static view of society as something merely to be maintained, and adopt a more dynamic conception of statesmanship as something active, progressive, and experimental, reaching out towards new powers for human activity and new conquests for the human will

W TROTTER, FRCS, FRS, *Instincts of the Herd in Peace and War* London T Fisher Unwin 2nd ed 1919 By permission of Ernest Benn Ltd

"Socialised gregariousness," Trotter concluded, "is the goal of man's development A transcendental union with his fellows is the destiny of the human individual, and it is the attainment of this towards which the constantly growing altruism of man is directed"

* * *

At the beginning of the war everyone seemed to have a new object in life People still came to the doctor, but they came with real complaints, like rashes or coughs During the Phoney War things got back to normal, however, and they were soon sending for the doctor with their usual freedom After the fall of France, people who got ill got well again quickly, to be ready for the invasion, I suppose. But gradually, as the months and years went by, depression set in People could not sleep, they were restless, they got headaches, they were nervy, they were on edge, waiting When D-day came things improved for two or three months; and then, in the late autumn of 1944, a general deep depression came down like a blanket The symptoms were uniform "I think it's my nerves, Doctor" "I go to sleep about two or three and then I wake up and can't sleep after" "I stay awake till five or six every night, and am fit for nothing next day" "I just want to cry when anyone speaks to me" A few patients attempted to find the cause of their worry "It's the war—it's been on so long," "It's all due to the bread" To the question "Do you worry much?" the answer was nearly always "Yes," but qualified in a large proportion by the words "But I've nothing much to worry about My husband is stationed near", or, from older women, "My sons are all stationed in England, so there's no need to worry" Most of the patients were women, and those who had real cause for depression—whose relations had been killed or taken prisoner, or who had themselves been blitzed—were in the minority. Physical signs were scarce—a few were anæmic, some had lost weight, and nearly all were flatulent None seemed to develop peptic ulcer The depression became so intense that it got alarming And this thing was so common casual acquaintances admitted to feeling depressed, friends gave fuller and more intimate details Some tried to cure themselves, one woman never got up until about midday "There is nothing to get up for," she said Another took a large number of music pupils after her day's work, and got only 5–6 hours' sleep a night Another regularly studied until about 3 AM and then rose at 7 30 AM Two others spent all their spare time cutting wood in the garden till tired out All except the first were doing far more in their ordinary day's work than they had done in peace-time Few asked for "a rest on the panel"; instead they asked for a nerve tonic With VJ-day the cloud certainly lifted, but now it is gradually descending again The story is changing slightly. "The war is over and I know there is no need to worry, but I can't help it" "I just want to howl I don't know why, because I have no worries" "The war hasn't worried me, because lots of us haven't known there has been a war on down in Devon I have just had a holiday, and yet I feel depressed" I prescribe sedatives and talk encouragingly, but it seems only palliative Perhaps a psychiatrist might help, but ideally he should be a psychiatrist who has endured and cured this depression in himself, and I have yet to meet him

* * *

When some of our grander colleagues talk derisively of the "stock bottles" of the harassed colliery or country practitioner, and laugh at the dispensing of stomach mixture, chest mixture, tonic mixture, and so on, they forget that not every village has an apothecary near at hand And they would do well to remember the saying about a beam and a mote How do they look nowadays to the outside observer when they hand out sulphonamide tablets with confident gaiety to any case savouring of an infective process? Besides, does the stock mixture really differ so much from the personal prescription meticulously written out on headed paper? Garnered as it usually is from the well-considered repertoire of a modern textbook or article, and nicely camouflaged by the manufacturers, the stock mixture may be the better agent It certainly wins on taste. and for the patient that means a lot

* * *

A German doctor, in charge of a POW ward, who has served in Russia for two years and says with apparent sincerity that he adores Russians, described the first news they had of penicillin towards the end of 1944. All captured British personnel were questioned, and it was finally decided that it was all one big bluff How could the British have found a substance that destroyed bacilli, cocci, and spirochætes? It was fantastic even Ehrlich was never as optimistic as that. After he had been with us for a few months and seen wounds heal with monotonous regularity he decided penicillin was the goods after all Up to date he has not claimed that Fleming was a German.

* * *

I took the family to the sea the other day for a picnic. Our preparations for this expedition were austere and simple, and I thought hungrily of the directions for picnics which I recently found in an old Victorian book, *The Etiquette of Modern Society* After advising the organiser of a picnic to hire a sufficiency of flys to carry his guests to the "trysting place," or to arrange for the railway officials to provide sufficient and comfortable accommodation on the "train selected," not forgetting the servants who are "convenient or even essential," the author dilates upon "appropriate comestibles," advising that at least the following should be taken "Cold chicken, ham and tongue, rolls filled with lobster salad or plain salad, sandwiches made of pounded chicken or game, foie-gras either made into sandwiches, between thin slices of dry toast, or a mouthful ensconced in a tiny shape of aspic jelly, cold salmon, abundance of salad [rather keen on salads, this chap], plenty of fruit, bread, butter, and cheese, quantities of ice, and no stint of claret cup, champagne, and cider cup, pies of boned pigeons, and some Devonshire cream for eating with fruit or tarts" After the frank statement that "luncheon is generally a somewhat prolonged entertainment," the author advises that the party disperse "to visit ruins, to walk to a waterfall, or to climb an elevation to see the view," adding that, after these "operations" as he calls them, the party should reassemble to dispatch "well iced claret and cider-cups and any fruit that may be left" The costume must suit the occasion The young ladies if it be chilly are counselled to wear "mohair, ticking, or serge," while the older ladies are warned against "elaborate trimmings and costly lace." As for the males, shooting jackets and wideawakes are said to be quite permissible, though frock coats and tall hats, it is hinted, are worn by those who aspire to be really well dressed

I would like to see Groucho Marx, in shooting jacket and wideawake, his lady on his arm, weaving his way to the waterfall, after such a luncheon, or all the brothers entertaining their guests in the ruins.

* * *

It is just 200 years since we English began to take the Scot We may have gained thereby as much as the Scot except for "usquebaugh" and "gowf," the former which has weaned many from the national drink of Britain while the latter has compelled the few to keep their feet on a bit of gutta percha while taking a walk, instead of revelling in the beauty of the countryside But even golf has had its good side in preserving as a green belt near our towns land that otherwise would have fallen a prey to the jerry-builder

Letters to the Editor

RENAL ANOXIA

SIR,—I have read with great interest the article by Aegraith et al in your issue of Sept 8, for I have long old that renal anoxia can produce a syndrome such as ney describe, though certain of the diseases with which ney associate the syndrome (yellow fever, blackwater ever, cholera) are outside my personal experience I iffer from them, however, in my views as to the probable ause of the renal anoxia, for I believe it to be the result f overstimulation of the vascular nerves, while they tribute it to peripheral circulatory failure and conseuently advocate blood transfusion as the best means of reventing lasting damage to the kidneys In a number f cases, such transfusion has not only been proved *ineffective, but has even been regarded as responsible* or the development of the syndrome

The matter is of such importance that I feel I should ate briefly how I have arrived at my opinions, though in letter such as this I must omit much of the clinical xperience which supports them

Since 1936 I have been collecting data about renal ailures consequent upon traumata, and have attributed hem to interference with the blood-supply—i.e, to enal anoxia Because of my previous work on the planchnics (*Rev Med Barcelona*, 1935, 24, 412, *Giorn. ital Anest Anal.* 1935, 1, 476), I have ascribed the nterference with the blood-supply to persistence of the rterial spasm which accompanies the very early stages f shock. *That the renal (and other) arteries can be* verstimulated reflexly or centrally, in unduly susceptible ersons, is suggested, for example, by the development of nuria through irritation of the ureter, or by the findings hysterical anuria (Osler and McCrea, Modern Medicine, ol v, p 489)

My method of treatment of war wounds was introuced, in part, with the object of lessening the danger f reflex arterial spasm and consequent distant, as well as ocal, anoxia To prevent the occurrence of gas-gan rene, I also stressed the importance of removing muscular issue which, in consequence of the trauma, had had its lood-supply unduly reduced and was therefore a poten ial culture medium for *Clostridium welchii*

When the crush syndrome was being widely attributed o the absorption of toxic substances produced at the site f the injuries, I was not convinced, and recommended he application of plaster casts to the crushed limbs to revent shock and consequent renal failure (*Brit med J* 940, ii, 502) In conjunction with J M Barnes I howed experimentally (see *Brit J Surg* 1942, 30, 74) hat widespread arterial spasm could be produced by a ocalised trauma in one leg, and we suggested that, lthough the leg muscles apparently recovered fully, ill ffects of a more lasting character might well be produced ere the reflex spasm to extend to vessels supplying more ital organs

The views to which I had been led were later accepted y Darmady, Scott, and their associates with whom I ad discussed the matter, and incorporated in their paper *Lancet*, 1944 ii, 609)

With certain colleagues, I have lately begun what we ope will be a full-scale experimental study of the effects f direct central, and reflex stimulation of vascular erves upon the various organs of the body If such timulation produces lasting pathological changes in the idneys and elsewhere, we shall then repeat the experi ents with appropriate nerve-blocking, &c, in order to iscover the best means of prevention of the undesirable ffects of overstimulation of these vascular nerves

Oxford J TRUETA

ACUTE SINUSITIS AND OTITIS MEDIA

SIR,—You plead for the use of sulphonamides with ection and careful observation (Sept 15, p 341) Hargrove, describing cases of frontal sinusitis and tis media, implies the same thing (p 335) Both peal for a saner view than emerged from an otological cussion at the Royal Society of Medicine some months

Putting prejudice aside, I believe that any otologist more than a few years standing might from the pre lphonamide era, parallel such cases as Mr Hargrove's. Without doubt sulphonamide therapy makes it necessary to tighten up our canons of recovery, bearing in mind that a blood borne drug chiefly benefits those parts of the lesion still retaining a good blood-supply Much has been written recently about deafness following sulphonamides, though little of it shows critical review of evidence Deafness has followed transient otitis media before, and so has brain abscess, and they will do so again, with or without drugs. In either event we are at fault only if culpably neglectful in assessing treatable pathology

In the ENT department at the Royal Victoria Infirmary, Newcastle-upon Tyne, we have a useful but not inflexible rule that an otitis which has "recovered" with sulphonamide stays in hospital longer than a case which has reached the same clinical picture spontaneously In the spate of writing on this subject I have yet to find a case not advertising that recovery was apparent rather than real; but, as for me, I have "missed" just as great a proportion of cases without as with chemotherapy I once sent out a case of cerebral abscess undiagnosed at a time when that disease was my particular hobby, and sulphonamides had nothing to do with the error

Newcastle upon Tyne FRANCIS MCGUCKIN

RESEARCH

SIR,—Your leading article of Sept 15 will be welcomed as a clear exposition of the value of group investigation

As many young research workers hope to gain their higher scientific degree (D SC), universities in this country would do well to change the conditions of its award Most British universities if not all, insist that a thesis submitted must be the result of the work of *one* individual For example, one university states "the degree will not be awarded solely on the evidence of work done in collaboration"

The day of the solitary worker in an attic or basement, with limited money and facilities, is passing University authorities should recognise this and alter their regulations to meet the requirements of the individual in a team

Llandough Hospital, Cardiff. DAVID G MORGAN

PURULENT MENINGITIS

SIR,—Your issue of July 14 has only just come to hand, but not, we hope, too late for comment on Dr Shalom's article on the treatment of purulent meningitis

In the first part of this he argues that obstruction of CSF flow occurs at the foramen magnum via the mechanism of medullary and cerebellar pressure cone He suggests that as in one case ventricular tap caused infected fluid under increased pressure to flow from a spinal tap previously clear and of low pressure, this relief of supratentorial pressure must have cleared a blockage at the foramen magnum But this result might equally follow relief of blockage at the tentorial hiatus or the foramina of Luschka The argument that there must have been free communication through the basal cisterns between proved infected right ventricular fluid and assumed infected fluid present over the meninges above the tentorium "as the patient was in a relapse of meningitis" is only justified by a misconception of the pathology of pneumococcal meningitis, which is essentially a meningo encephalo-ventriculitis once the process has become well established In partially treated cases localisation of infection anywhere in the ventriculo subarachnoid space may occur Spread of infection to the whole space or any large part of it will then cause clinical relapse The pressure cone mechanism in tumours which he quotes is a late pre mortem effect, at any rate where blockage is complete or marked Were it operative to any extent in these cases, the picture would be rapidly progressive and hastened by any attempt at lumbar puncture In fact, post mortems show it to be slight (though tentorial coning is more marked) and demonstrate clearly the blockage of the foramina and cisterns in the route of CSF circulation These mechanisms would adequately explain the facts he quotes.

He next attempts to show that intramuscular 20% dextrose solution encourages circulation of penicillin from lumbar to intracranial fluid The evidence is first that the inhibitory power of lumbar CSF following intrathecal penicillin falls more rapidly when an intra

muscular hypertonic solution is given after the penicillin In one observation the inhibitory power fell to nil 3 hours after injection, but by 24 hours inhibitory power had returned From this he suggests that the penicillin, aided by the hypertonic injection, had passed into the cerebral CSF and then returned to the spinal theca As no observations were made on the inhibitory power of the cerebral fluid at the relevant times, the whole argument remains suppositive, and, drawn from one observation on one case, is scarcely sufficient basis for the claim that penicillin does not behave as a solute Further evidence is drawn from the effects of intramuscular dextrose on pulse-rate and mental responsiveness In his graph of this, if the time markings are correct, the effect is just as rapid and as marked with intramuscular as with intravenous solutions, and on at least one occasion the injection was followed by coma and a drop in pulse-rate The remarkable occurrences and recessions of 7th nerve palsy he also considers due to changes in intracranial pressure This view does not appear to be supported by the behaviour of 7th nerve function with other causes of raised intracranial pressure, such as tumour or basal arachnoiditis

The importance of adequate circulation of intrathecal penicillin has already been stressed in papers both experimental and clinical It would be unfortunate should Dr Shalom's article, or the authority you lend it in your subsequent annotation, lead anyone to withhold penicillin by the ventricular route where there is evidence of blockage in the cranio-spinal circulation and lack of response to intraspinal treatment

R P JEPSON
CMF C W M WHITTY

IS THERE A SHORTAGE OF DOCTORS?

SIR,—Both Dr Butcher and "Young Surgeon" seem to me to be talking nonsense My experience, and that of other doctors of my acquaintance, is that it is impossible to get a satisfactory locum or assistant

I have been able to have three days' holiday since 1938, when I had one week, and I have, of necessity, gone on working with influenza

The only locum I have been offered for any reasonable time was a German-Pole who required every comfort, exorbitant fees, and little work.

Worksop, Notts GAVIN DUNLOP

ARMY MEDICAL SERVICES

SIR,—I have just read Lieut -General Sir Alexander Hood's Harveian lecture published in your issue of June 5, and even at this late date would like to comment on it

The Army does provide a total health service and in theory it is admirably organised, but, as will be agreed by many who, like myself, have spent the last six years in the RAMC, in practice it falls short of the ideal The reasons for this failure ought to be considered seriously at present because of their bearing on the planning of a National Health Service In my opinion they are as follows

(1) In the Army authority and responsibility are not delegated sufficiently to medical officers in junior posts This results in an enormous amount of paper work over details, with irritating and hampering restrictions and delays, besides occupying the time of senior officers which should be given to wider problems A further consequence is that officers become unaccustomed to responsibility, and later unable to exercise it, so a vicious circle develops

(2) Promotion and appointments often go primarily by seniority and only secondarily by merit This results in posts not being filled in the most efficient way, which is naturally reflected in the efficiency of the Service as a whole Many administrators in the Army do not possess the admirable qualities that Sir Alexander Hood gives for the holders of such posts

(3) Either the attractions of the regular Army Medical Service have not been great enough to obtain a sufficient number of really able medical graduates—as administrators or clinicians—or the amount of work provided in peace time by the Service is not sufficient to provide the necessary administrative and clinical experience The result is a lack of interest in the efficiency of the Service and inability to cope with its war time problems

In spite of these criticisms, in my experience the medical service provided by the Army both at home and abroad under difficult conditions is far better administratively and clinically than that provided in some areas by the EMS

In brief, the efficiency of a service depends not only on its organisation but also on the men who run it and how they interpret it

Rydal, Westmorland K COBBAN

MITRAL STENOSIS AND SILICOSIS

SIR,—As a corollary to your annotation of June the following case may be of interest It was diagnosed as silicosis with cardiac embarrassment, but autopsy showed only mitral stenosis of the buttonhole type

A married man, aged 39, was admitted to hospital on March 26 complaining of dyspnœa on exertion and attacks of severe nocturnal dyspnœa over the past two years At the age of 16 and again at 18 he had "pneumonia"—febrile attacks of sudden onset, accompanied by a cough and some sputum Between the ages of 20 and 30 he had "pleurisy" 5 or 6 times—illnesses characterised by pain in the chest accentuated by coughing He had had "bronchitis" for as long as he could remember, using this term for frequent chest complaints He had no history of sore throats or rheumatic fever, though his father had died of rheumatic endocarditis at the age of 59. Two years ago he began to get dyspnœa on exertion, and on one or two nights each week awoke breathless and uncomfortable The dyspnœa at first limited and later abolished his capacity for work, while in hospital he could only walk 20 yards on the level, and was unable to climb stairs He had no pain in the chest and but a slight cough with little sputum, never blood-stained He had smoked 30–40 cigarettes a day between the ages of 20 and 35, but since had smoked less than 10 a day

At the age of 14 he left school and was a bricklayer for 15 years In 1935 he was put in charge of the sandblasting machine for periods of 2–6 hours each day Masks were provided, but owing to the difficulty in breathing and inconvenience caused by them, he seldom wore one In 1940 he was taken off this job, and turned to carrying bricks Within a year he had to give up owing to breathlessness, and in October, 1944, stopped work altogether

On admission he was pale and slightly icteric Weight 9 st 8 lb, height 5 ft 8½ in, temperature 98° F, pulse-rate 100, respirations 22 per min, blood-pressure 110/80 mm Hg He had three carious teeth His chest was symmetrical, with expansion limited to 1½ in The anteroposterior diameter and thoracic curve of the spine were increased, the costal angle wide and fixed The whole chest was resonant on percussion, and breath sounds were vesicular, distant, and dry, some diffuse sibilant and sonorous rhonchi almost disappeared after a few days' rest in bed, there were no râles The fingers were slightly clubbed and cyanotic The apex beat was in the 5th interspace, just lateral to the midclavicular line; trachea central, neck veins not visibly distended, arm and leg veins emptied slowly when the limbs were raised A soft blowing systolic murmur was heard at the apex, fading towards the midline and reappearing over the tricuspid area, no palpable thrill Superficial liver dullness extended to three-fingers' breadth below the costal margin, liver neither pulsatile nor tender

The urine contained no sugar or albumin Red cells 5,140,000 per c mm, Hb 98%, CI 0 95, white cells 6800 per c.mm (polymorphs 50 7%, lymphocytes 31 7%, monocytes 9%, eosinophils 5 7%, basophils 3%) X-ray films showed diffuse fibrosis of the lung, with cardiac enlargement, the pulmonary conus was not enlarged An electrocardiogram showed regular auricular and ventricular rates of 100 per min, P-R interval 0 13 sec, P_1 prominent and notched P_2 and P_3 prominent, much right preponderance, T_2 flat, T_3 inverted

Silicosis with right ventricular strain was diagnosed and the patient was sent out on April 13 for further convalescence On April 27 he was readmitted with severe congestive heart failure and gross purpura in dependent tissues, having had a severe cold and an attack of diarrhœa His condition deteriorated rapidly, and he died on May 7

Autopsy revealed no macroscopic features of silicosis The lower lobes of both lungs were collapsed, and the pleural cavities contained much straw-coloured fluid Several infarcts were seen, mostly in the right lung The bronchi showed chronic inflammation The heart weighed 420 grammes; right ventricle enlarged Mitral valve admitted

the tip of the little finger only; flaps adherent, fibrotic, and calcified. A calcified ridge surrounded the valve ¼ cm from its edge. A few small vegetations were present. The left ventricle was slightly dilated. The aortic valve appeared normal, the tricuspid valve relatively incompetent. Average thickness of both right and left ventricular walls was 1·3 cm; circumference of the tricuspid valve 11 cm., of the mitral 4·5 cm. Nutmeg liver with gross fatty degeneration; spleen congested; stomach and intestines œdematous. Histologically the lung showed a fine fibrosis and passive venous congestion, with some emphysema; no evidence of silicosis.

During the clinical examination the possibility of silicosis, suggested by X ray films, was supported by the appearance of the chest and the gradual limitation of the patient's capacity for work. The history of exposure supported the diagnosis, though it was recognised that the cardiac condition was important.

The patient at 39 was as likely to show the effects of industrial hazards as of rheumatic fever. In the absence of a history of rheumatic fever weight was given to the occupational history; and though it is unusual for silicosis to appear after 5 years' exposure in some trades (granite quarrying, coalmining), in others, including sandblasting, less than 5 years' exposure will produce it. Radiographic differentiation is not absolute, but shadows cast by vascular congestion tend to fade towards the periphery of the lung, and to be more definite in the right lung, and this was so in our case.

Since the findings were equivocal, we looked to the heart itself for guidance, and this proved misleading. Right ventricular preponderance was proved, but characteristic mitral murmurs, fibrillation, gallop rhythm, heart-block, and haemoptysis were all absent. True, the patient was orthopnœic, though he denied it, but the diagnosis could have been established only if silicosis showing reticulation could be excluded as a cause of such a degree of congestive heart-failure. Cardiac embarrassment is not a constant accompaniment of silicosis, and it is agreed that severe embarrassment does occur; but is late, not appearing until X ray films show conglomerate or coalescent foci in simple silicosis, or a superadded infection.

It therefore seems that mitral stenosis with congestive failure can be distinguished from silicosis on clinical and radiographic appearances, even in the absence of mitral signs. Coalescent nodulation could not be simulated by pulmonary vascular congestion, and in its absence it can be assumed that the silicosis is not sufficiently advanced to produce congestive failure.

Thanks are due to Prof. W. H. Wynn, FRCP, for permission to publish this case, and to Dr. W. T. Cooke for advice and criticism.

Birmingham University Medical School. D. A. HANSON

PENICILLIN TREATMENT OF GONORRHŒA

SIR,—An investigation was carried out at this centre to assess the relative values of penicillin in oil and penicillin in water, in the treatment of acute gonorrhœa. Of 129 cases used in the investigation, 74 received the penicillin-oil preparation and 55 the penicillin water preparation. The cases were selected, in so far as no case with a history of exposure to infection of over two weeks was recorded.

The penicillin water preparation was made by dissolving 100,000 units of penicillin sodium in 2 c.cm. of sterile water. The penicillin-oil preparation was made by extracting the penicillin sodium from the ampoule with 6 minims of sterile water and then dissolving this in 3·5 cm. of a 1% solution (sterile) of beeswax in arachis oil. The beeswax in-oil solution was sterilised by autoclaving and then cooled to 0° C. in a refrigerator before solution of the penicillin. The mode of administration was one intramuscular injection of 100,000 units of penicillin into the gluteal. Each case was seen daily and the character of the urethral discharge noted. Urethral smears were taken at any stage and the urine (two-glass test) was examined daily. A patient showing a positive urethral smear (GC +) at any stage after the injection was regarded as a failed case. Any patient showing the slightest sign of a mucopurulent discharge on the second day after treatment was regarded as a failed case. The relative efficacy of treatment was assessed by the number of days spent in hospital by each patient. Full investigation by sounds and prostatic examination was done in all cases.

The results were as follows:

	(A) PENICILLIN WATER	(B) PENICILLIN-OIL
Cases treated	55	74
Failed cases	5	5
(%)	9·09	6·38
Av. no. of days in hospital (excluding failed cases)	4·2	5·1

From the results it would appear that penicillin in oil has no advantage over penicillin in water in the treatment of acute gonorrhœa.

A high initial concentration of penicillin in the blood is apparently the important factor in therapy.

Clinically, the slower rate of absorption of penicillin from the oil preparation was demonstrated by the persistence of a urethral discharge on the day following injection, whereas most of the penicillin water cases showed no discharge from the urethra.

My thanks are due to Brigadier Cormack for permission to publish this investigation.

Kenya. K. B. WOOD

HYPOPIFSIA

SIR,—I regret Dr. Watson Smith's letter because I fear that this expression of the views of an experienced and distinguished physician may perpetuate an already too prevalent blood pressure neurosis. For some years past I have noticed that approximately two thirds of my patients remark, as I apply the sphygmomanometer cuff, "I'm afraid you will find it too low, Doctor." There seems to be a widespread delusion that a pressure of 120 in a subject of forty to fifty is pathological, and that in an individual of any age a pressure of or below 110 calls for alarm and despondency.

I submit, Sir, that, in the absence of evidence of organic disease, systolic pressures as low as 100 can and should be disregarded, and that on no account should the patient's symptoms be attributed to them. Particularly is this the case just now, when six years of war are giving place to a somewhat dreary peace, and we are beset by exhausted and anxious patients in whom courage is not engendered if their prostration is explained on a basis of "low blood pressure." Remember also that to the average layman the diagnosis of "low blood pressure" or, more pernicious still, "tired heart," means heart disease and possibly sudden death.

I agree profoundly with Dr. Watson Smith in the futility of attempting to raise the hypotensive pressure by "galenicals" and I cannot help thinking that Dr. Watson Smith's abdominal belt, with its perineal thong, acts more by suggestion than by any circulatory influence. I can, however, well believe that many of his patients "cling to the belt tenaciously and for long." Even so did the visceroptotic neurasthenics cling to their an comfortable abdominal trusses long after we had learned that their symptoms, but not their visceroptosis, were relieved thereby.

London MAURICE CASSIDY

News has reached this country that Dr. CICELY WILLIAMS is among the prisoners liberated at Singapore. She writes that she is "remarkably well" and that she may stay on for another two months to help to get the medical services going again. Dr. Williams was first imprisoned in Changi Camp and later was one of the 50 men and 3 women moved to the Gestapo prison attached to the camp where she spent 5 months. But since March she has been at the Syme Road Camp.

NEW DEAL FOR WATER.—The Water Act 1945, which comes into force on Oct. 1, makes it the duty of the Ministry of Health to promote the provision of an adequate water supply for every householder. It also simplifies and expedites the procedure by which bodies supplying water can gain the powers they need for carrying out their task, besides making it easier for them to combine for joint action, execute work and obtain land and water resources. The Minister can now conserve water in any suitable area and prevent its waste and misuse, and he has powers to unify by laws against pollution. Agricultural needs and the need of new housing estates will be specially considered. (See Lancet July 7, 1945, p. 17.)

Obituary

JAMES HENDRY.

MBE, M A B SC, M B GLASG , F R C O G

Dr James Hendry, regius professor of midwifery in the University of Glasgow, who died on Sept 9 at the age of 59, combined a deep devotion to his work with an impersonal attitude towards the good of medicine and of his own specialty He served his university and his profession with generosity and wisdom

Born in 1885 at Beith in Ayrshire, he went in 1903 to the University of Glasgow, where he was a notable secretary and later president of the students' representative council In 1910 he graduated in the faculties of arts, medicine, and science, and after acting as Muirhead demonstrator and assistant to the professor of physiology he went abroad to continue his studies in Austria, Germany, and France He had but shortly returned to Glasgow when the war of 1914 broke out, and for his services during the next two years as adjutant to the university officers' training corps he was awarded the MBE In 1916 he was posted to France where he served with the rank of major till 1919 Back in Glasgow once more, he took up his work as surgeon and teacher, and was soon appointed to the staff of the Royal Maternity Hospital, where he was later chief obstetric surgeon He also became gynæcologist to the Glasgow Royal Infirmary. In 1919 he had been made first assistant to the Muirhead professor, and eight years later he succeeded Prof. Munro Kerr in the chair To this period belongs his joint authorship of *Notes on Midwifery* for students (1920) and the *Combined Textbook of Obstetrics and Gynæcology* (1923) To all his patients he showed the same uncompromising thoroughness tempered with kindness and gentleness, but when he succeeded to the regius chair two years ago he gave up his private practice and continued his clinical work as medical director of the Royal Maternity Hospital and Women's Hospital The students of Edinburgh, Aberdeen, Durham, and Belfast knew him as an external examiner

Whatever Hendry did filled his whole mind and took all his energies ; but this did not mean that his interests were narrow He was deputy chairman of the Central Midwives Board for Scotland, chairman of the Scottish medical advisory committee of the Nuffield Provincial Hospitals Trust, a member of the medical advisory committee of the Secretary of State for Scotland, a member of the court of his university, and a foundation fellow of the Royal College of Obstetricians And on none of these bodies was he a passenger. From his busy life he stole time—no-one knew how—to study both the general situation and the particular point on which his experience entitled him to speak with authority He would go to great trouble to check his data and he had the knack of presenting them clearly and lucidly so that they were readily seized by the lay and medical members of his committees And the deductions he made from his material were wise and far-seeing As the representative of his specialty on the Goodenough Committee he had often a difficult task, for in many centres the teaching of midwifery is hampered by a lack of teaching material, and he had to balance the students' needs with those of midwives, taking account of the trend towards institutional midwifery When he made any recommendation his only touchstone was the good of medicine ; he was selfless about his own position and was ready indeed to be ruthless about difficulties raised for reasons he thought less altruistic

Speaking at a memorial service Sir Hector Hetherington principal of Glasgow University, summed Hendry up as a man of great natural gifts—" tireless energy, a wide, exact, and beautifully ordered memory, so that he could bring to bear on any situation the full range of his experience and knowledge, a cool and balanced judgment, executive skill of the highest order And with these, kindness, patience, good humour, forthright honesty of purpose and of speech "

Professor Hendry married in 1914 Miss H L Williamson who survives him with three sons

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Prof R P LINSTEAD, D SC, FRS, has been appointed director of the chemical research laboratory in the Department of Scientific and Industrial Research

On Active Service

CASUALTIES

WOUNDED

Captain J G A GILRUTH, MRCS, RAMC
Captain J. A PERFOLI, MC, LRCPE, RAMC
Lieut -Colonel J M SCOTT, MB LOND , RAMC

AWARDS

BAR TO AFC

Wing-Commander J P HUINS, OBE, AFC, MRCS

CBE

Brigadier HAROLD EDWARDS, MB LOND , FRCS, RAMC
Colonel T D INCH, OBE, MC, MD EDIN , RAMC

DSO

Lieut Colonel A T MARRABLE, MRCS, RAMC

OBE

Lieut -Colonel W N J CLARKE, MB, RAMC
Colonel DEV DATT, MB ST AND , IAMC
Lieut -Colonel R T GRANT, MD GLASG , RAMC
Colonel JOHN KINNEAR, MB ST AND , RAMC
Lieut -Colonel J A MACDOUGALL, MD MANITOBA, RAMC
Lieut Colonel F H TAYLOR, MD DURH., RAMC
Lieut Colonel A W S THOMPSON, MB EDIN, RAMC
Lieut -Colonel E S WATSON, MB EDIN , RAMC
Colonel G M WARRACK, DSO, LRCPE, RAMC

MBE

Captain ISAAC CAMRASS, MB GLASG , RAMC
Major JOHN LEIFER, MB L'POOL, RAMC
Major K C MALLEN, MB NUI, RAMC
Captain JAMES MCLEAN, MB EDIN , RAMC
Major E R R MELLON, MB LOND , RAMC
Major A S RAMSEY, MB BELF , RAMC
Major F E WHEELER, FRCSE, RAMC
Captain A W LIPMANN KESSEL, MRCS, RAMC

MC

Captain G R EVANS, MB LOND , RAMC
Captain M S HOWE, MRCS, RAMC
Major F I EVANS, MB CAMB , FRCS, RAMC
Captain E B NAUG, MB, IAMC
Captain A W. LIPMANN KESSEL, MRCS, RAMC

MEMOIR

Captain JEAN NELSON was born in 1915, the second daughter of Mr Nelson and the late Mrs Nelson of Buckland, near Aylesbury At Wycombe Abbey School she was head of her house and school captain In 1939 she took the Conjoint qualification at University College Hospital, and she spent the first three years of the war in the Emergency Medical Service, working as an anæsthetist at University College Hospital, and later as house physician at Hemel Hempstead, Stanmore, and Ashridge In the autumn of 1942 she joined the RAMC, and after serving with an anti aircraft division, she was posted to France with the BLA in the summer of 1944 After a short spell she returned to England, and was almost immediately sent to India From Delhi she was moved to the Central Military Hospital at Agra, where she died on Aug 15 from infective hepatitis " Always a gay and sympathetic companion," writes N W , " Jean Nelson faced the troubles that came to her latterly with cheerful courage which we all admired, and spread an atmosphere of friendliness and happiness among her friends and patients "

Yeandi

BRITISH ORTHOPÆDIC ASSOCIATION —A meeting will be held at the Royal College of Surgeons of England on Friday and Saturday, Oct 26 and 27. Further information may be had from the secretary at 45, Lincoln's Inn Fields, London, WC2.

Notes and News

NURSES FOR THE COLONIES

A REPORT on the training of nurses for the Colonies (Cmd 6672. H.M Stationery Office Pp 65 1s) comes from the committee who under the chairmanship of Lord Rushcliffe have been studying this subject since November, 1943 They point out that no great extension of nursing services could have taken place in the Colonies unless the greater part of the nursing staff had been drawn from native populations; and they make suggestions for training girls and male nurses along practical lines so that they can teach their own people, even after they give up nursing as an occupation

They recommend that nurses recruited in the Colonies should be trained locally in training schools, and that the standard should be such as would render Colonial certificates acceptable to the General Nursing Council of England and Wales for State Registration This is a little difficult to reconcile with their finding that the general education of girls is backward in most Colonies, and the suggestion that in some backward areas there should be two grades of nurse, those in grade I to take the full training those in grade II to be taught the same subjects "but with a smaller content, precepts being inculcated by practical demonstration rather than by lecture" They feel, however, that general as well as professional education may be improved by appropriate pre nursing courses

A four year training in nursing is proposed, three years being occupied in basic studies including elementary general science anatomy, physiology, hygiene domestic science, nutrition and dietetics, maternity and child welfare, the theory and practice of the various branches of nursing, first aid, pharmacology and therapeutics, psychology social science, and methods of health education With such a wide programme before her, the candidate will probably feel thankful her training period is no shorter Her fourth year is to be *spent in training in the special branch in which she* wants to nurse, and it is encouraging to note that the training in "community nursing" on the lines proposed by Dr Janet Welsh (see *Lancet* 1941, ii, 574) is given special prominence Midwifery training is also to follow the English pattern.

The report proposes that nursing and midwives' councils should be set up in each territory to maintain standards of training, and that nurses who qualify in the Colonies should be given the chance to attend refresher courses and also to come to England for postgraduate training if they seem likely to profit by it Other recommendations foreshadow experiments in joint training colleges for students of nursing and teaching—a plan that might be worth considering in our own country

In the training of British nurses planning to work in the Colonies they suggest more emphasis on the preventive outlook, and a special course of instruction to fit them for work abroad They urge nurses to 'take every opportunity of learning the principal language of the territory in which they are to work" but as things are at present such opportunities must be negligible until the nurse arrives at her station

The committee rightly look towards an expanding and improving service, and have made recommendations in keeping with that hope But their report does provoke the reflection that the British pattern has perhaps been taken too confidently as a model May not the circumstances in different Colonies call for a more elastic framework with greater liberty for experiment? There is always a danger that experience gained in one field may be applied too lightheartedly in another Even Florence Nightingale it will be remembered took a lot of convincing that the windows of Indian hospitals should be kept closed, not open

THE MIDWIFE AND THE MINNITT

UNDER the regulations of the Central Midwives Board the midwife has for some years been allowed to give women in labour gas and oxygen analgesia with a Minnitt or similar apparatus, provided that she has been properly instructed in its use, that a doctor has certified the patient fit to take gas and oxygen and that a third person with certain specified qualifications is present The third person had to be one of the following: a state-certified midwife a state registered nurse a senior medical student a pupil midwife a retired midwife, or 'a woman over 21 years of age the regulation runs, who is and has been for at least a year either a VAD or ordinary member of the British Red Cross Society or the Order of St John or an enrolled member of the Civil Nursing Reserve The Central Midwives Board has several times approached the Royal College of Obstetricians and Gynaecologists with a view to getting these somewhat stringent requirements changed for at a time when those with any kind of nursing qualification are at a premium, few can spare some hours to attend a confinement in the rôle of looker-on and medical students and pupil midwives are not always at hand The upshot has been that many women have had to bear their labour pains uneased by the reasonably safe and simple technique possible with the Minnitt apparatus The College has now agreed to a change in the regulations, and from Sept 1 onwards midwives have been permitted to give gas and oxygen analgesia provided "one other person being any person acceptable to the patient, who in the opinion of the midwife is suitable for the purpose is present at the time of administration in addition to the midwife in charge of the case" This means that any sensible relative or neighbour whom the patient likes will be accepted; and the midwife will be in a position to relieve pain in childbirth as a matter of course

MEDICAL PLANS FOR AUSTRIA

THE Association of Austrian Doctors in Great Britain has published a collection of essays on medical reconstruction and reablement in Austria (*The Health Services in Austria Essays Collected by the Committee for Post-war Medical Relief in Austria* 14 Craven House 121 Kingsway London WC2 Pp 40 3s) As Prof F Silberstein says in his preface for the next few years Austria will need to train doctors as quickly and inexpensively as possible, and hopes of a lengthened medical course with a better grounding of all students in preventive medicine may therefore have to wait awhile

Dr A. Czech tells of the high standard in public health achieved under the leadership of Karl Seitz as lord mayor of Vienna The hospital service he says was equal to the public needs; there were antenatal clinics welfare and child guidance centres, and a marriage-guidance centre which was doing pioneer work. Young couples could apply as soon as their first baby was born for a municipal flat with labour saving equipment and good balconies in the larger blocks there were day nurseries, club rooms, and libraries, and all were provided with communal laundries National health insurance had been introduced in 1888, and included all people gainfully employed, regardless of income In the new service Dr Czech hopes to see greater emphasis on prevention

Maternity and child welfare were equally well developed Dr F F Tietze has some practical suggestions to make about the stocks of dried milk, cod liver oil, and concentrated orange juice likely to be needed during the coming winter and has worked out the quantities required by individual children of different ages as well as the bulk amounts for all Austrian children over a period of 26 weeks

Dr Erich Schindl has considered ways of making economical use of the doctors and specialists available and finds the best hope in the establishment of health centres offering free treatment to all residents in their area In the rural areas he suggests the mobile units introduced by the Nazis should be taken over and adapted for wider use Dr Felix Bauer and Prof M Schacherl have constructive suggestions to make on reablement physical and mental Dr A Fessler discusses a proposed campaign against venereal disease, and Mr W Nukides looks forward to a better dental service

This booklet is evidence of the knowledge and devotion with which these exiled doctors have been working for their country's reconstruction

HOT BOTTLES

SINCE hospital demands are falling off and production is already rising, the rubber hot water bottle is now on sale again to the general public Sick people and expectant mothers have first claim they need only present a medical certificate to an appropriate shopkeeper and he will get them bottles through his usual supplier Maximum retail prices have been fixed at 7s 2d and 8s 3d (according to size) for moulded bottles and 12s 11d for hand made bottles; but a substantial proportion of available supplies will be on sale at lower prices Those who have learned to patch nightly a leaking aluminium bottle with flour and water (which bakes into a vulnerable pie-crust over the hole) will await their next illness or pregnancy with enthusiasm

A limited edition of the WELLCOME MEDICAL DIARY for 1946 is now being printed, and will be distributed early in December Doctors who have not yet ordered their diary should apply to Burroughs Wellcome & Co 183 Euston Road, London NW1

Royal College of Surgeons of England

The following lectures will be delivered at the College in Lincoln's Inn Fields, London, WC2, at 5 PM, during October and November.

Imperial Cancer Research Fund lecture Dr Leslie Foulds, Cancer Research (Thursday, Oct 4).

Lister lecture Sir Howard Florey, FRS, the use of micro organisms for therapeutic purposes (Thursday, Oct 11)

Erasmus Wilson demonstrations Mr R Davies Colley, cysts and innocent tumours of the breast (Monday, Oct 22), malignant tumours of the breast (Wednesday, Oct 24) Mr L E C Norbury, the kidney (Thursday, Oct. 25)

Thomas Vicary lecture Sir Arthur MacNalty, the influence of the renaissance on English medicine, surgery, and public health (Thursday, Nov 1)

Bradshaw lecture Mr C Max Page, fracture treatment (Thursday, Nov 8)

Royal Institute of Public Health and Hygiene

Colonel Walter Elliot, FRCP, has been elected president of the institute in succession to the late Sir Stanley Woodwark.

Royal Society of Medicine

On Wednesday, Oct 3, at 2.30 PM, Sir Arthur MacNalty will deliver his presidential address to the section of history of medicine He will speak on the influence of medical poets on English poetry. On Oct 4 at 8 PM at the section of neurology Dr J Purdon Martin will give his presidential address on the discharging lesion

Welsh National School of Medicine

Dr J R Rees, medical director of the Tavistock Clinic, London, will give the opening address of the new session at this school on Tuesday, Oct 2

British Institute of Philosophy

On Monday, Oct 8, at 5 PM, at 14, Gordon Square, London, WC1, Prof C D Broad, LITT D, will speak on problems of moral philosophy

Liverpool School of Tropical Medicine

Courses of instruction for the diplomas in tropical medicine and tropical hygiene of Liverpool University are to be resumed The first course for the DTM will start on Jan 3, and the examination will be at the end of March A DTH course will start in April

Specialists needed for China

Medical practitioners with specialist experience are urgently required for immediate service with UNRRA in China as radiologists, gynæcologists, obstetricians, surgeons and orthopædic surgeons, physicians, otolaryngologists, pædiatricians, and ophthalmologists Particulars will be found in our advertisement columns

Return to Practice

The Central Medical War Committee announces that the following have resumed civilian practice

Dr BERNARD SCHLESINGER FRCP, Hospital for Sick Children (Private Wing), Great Ormond Street, WC1.

Mr A L D'ABREU, OBE, FRCS, Surgical Unit, Royal Infirmary, Cardiff

Mr C W GORDON BRYCE, 118, Harley Street, London, W1.

Mr GEORGE T. HANKEY, MRCS, LDS, 79, Harley Street, W1

Dr H. L MARRIOTT, FRCP, 63, Wimpole Street, W1

Mr R. K DEBENHAM, FRCS, 18, Greenfield Crescent, Edgbaston, Birmingham

Dr W S C COPEMAN, FRCP, 41, Harley Street, W1

Mr R. OGIER WARD, FRCS, 149 Harley Street, W1

Dr STEPHEN COFFIN, 52, Upper Brook Street W1

Dr J NORMAN CRUICKSHANK, FRCI, 4, Newton Place, Charing Cross, Glasgow, C3

Department of Industrial Ophthalmology

The Royal Eye Hospital, London, has established a department of industrial ophthalmology to which Mr J. Minton, FRCS, has been appointed ophthalmologist The following problems are being investigated

(1) Prevention of eye injuries (type and efficiency of preventive appliances)
(2) Welders' conjunctivitis (arc eye)
(3) Lens opacities in furnace workers, welders, and so forth
(4) Rehabilitation of the one-eyed worker
(5) Eye strain of workers engaged on fine close work (radio valve manufacturers; work on very fine parts in any other industry)
(6) Eye strain due to deficient illumination during work
(7) Keratitis conjunctivitis amblyopia, due to the use of industrial solvents (carbon tetrachloride, benzol, carbon disulphide, aniline dyes, and so forth)
(8) Vision and the selection of staff in industry (visual standards in industry)

Industrial medical officers are invited to refer any of these problems or any other difficulties in industrial ophthalmology to Mr Minton at the Royal Eye Hospital, St George's Circus, London SE1

Disabled Persons Register

The register of people entitled to the advantages provided by the Disabled Persons (Employment) Act was opened on Sept 25. As soon as it contains sufficient names the Minister of Labour will fix the quota of disabled which every employer of more than 20 workpeople must engage To begin with this will probably be 2%, but it will grow with the register Registration is voluntary and is open to those disabled through war service, industrial, road, or other accidents, or congenitally Disablements which do not carry a war pension may yet admit to the register, for disease is recognised equally with injury or wounds as a cause of disablement

INFECTIOUS DISEASE IN ENGLAND AND WALES

WEEK ENDED SEPT 15

Notifications —The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1381; whooping-cough, 1159, diphtheria, 495; paratyphoid, 15; typhoid, 17; measles (excluding rubella), 551; pneumonia (primary or influenzal), 326; puerperal pyrexia, 140; cerebrospinal fever, 39; poliomyelitis, 31; polio-encephalitis, 2; encephalitis lethargica, 3; dysentery, 292; ophthalmia neonatorum, 80 No case of cholera or typhus was notified during the week

The number of service and civilian sick in the Infectious Hospitals of the London County Council on Sept. 12 was 1025 During the previous week the following cases were admitted scarlet fever, 81, diphtheria, 28, measles, 15, whooping-cough, 23

Deaths —In 126 great towns there were no deaths from measles, 1 (0) from an enteric fever, 1 (0) from scarlet fever, 5 (1) from whooping-cough, 7 (0) from diphtheria, 77 (4) from diarrhœa and enteritis under two years, and 11 (2) from influenza The figures in parentheses are those for London itself

Blackburn reported the fatal case of enteric fever There were 10 deaths from diarrhœa and enteritis at Liverpool, and 9 at Manchester

The number of stillbirths notified during the week was 203 (corresponding to a rate of 30 per thousand total births), including 21 in London

Appointments

FOSTER-CARTER, A. F, DM OXFD temp. medical superintendent at Brompton Hospital Sanatorium, Frimley

CURRAN, D D, MB NUI RSO, Scunthorpe and District War Memorial Hospital.

CAVANAGH, FLORENCE, B SC MANC, MB MELB, DLO, part-time chief assistant, aural department, Manchester Royal Infirmary

GARSON, H L, OBE, MC, MB CAMB examining factory surgeon for Bebington, Cheshire

MORRIS, PATRICK, MRCS, DPM examining factory surgeon for Donington, Lincolnshire

COLONIAL SERVICE —The following appointments are announced
KNOWLES, ETHEL E A. D, MRCS DMO, Bahamas
MILLER, MARGARET D, MB EDIN MO, Tanganyika.
MUNRO, H A, LRCPE MO, St. Vincent.

Births, Marriages, and Deaths

BIRTHS

ATKINSON —On Sept. 16, at Romford, Essex, the wife of Dr Esmond Atkinson—a son

HUGH-JONES —On Sept. 20, at Poole, Dorset, the wife of Dr Philip Hugh-Jones—a son

MACKENZIE.—On Sept 20, at Wakefield, the wife of Capt. A G Mackenzie, RAMC (SEAC)—a daughter

PRICE.—On Sept 20, in London, Dr. Dora Price, wife of Squadron-Leader C F. Price, MB, RAFVR—a daughter

TEMPLE.—On Sept. 15, in London, Dr Barbara Temple (née Broadwood), wife of Captain L J Temple, RAMC—a daughter

WHITEHEAD —On Sept. 15, at Salisbury, the wife of Dr H L Whitehead—a daughter

MARRIAGES

ABBOTT—RANKIN —On Sept. 18, in Cyprus, Peter Harry Abbott, MRCS, Sudan Medical Service, to Mary Lucas Rankin

FULTON—ELLIS —On Sept 14, at Brockenhurst, Morris Fulton, MC, major RAMC, to Diana Lilis, third officer WRNS

MACARTHUR—WARDE.—On Sept. 20, at Ramsey, Archibald Alastair Cameron MacArthur, captain RAMC, to Elinore Muriel Warde, flight-officer WAAF

OWENS—MORTIMER.—On Aug 30, at Chittagong, Bengal, Walter Eugene Owens, major DIS, to Dorothy Joan Mortimer, QABDNS(R)

PEARSON—JOHNSTON —On Sept 18, at Cambridge, Alan Guy PEARSON, MB, Northiam, Sussex, to Beatrice M. Johnston

DEATHS

MCCUTCHEON.—On Sept. 17, at Selly Hill, Birmingham, Archibald Munn McCutcheon, MB GLASG, FRFPS, formerly medical superintendent of Monyhull Colony

PARRY —On Sept 21, in London, Thomas Wilson Parry, MA, MD CAMB, FRCS

CHRONIC FATIGUE

SIR ADOLPHE ABRAHAMS OBE, MD CAMB, FRCP
PHYSICIAN TO THE WESTMINSTER HOSPITAL; CONSULTING PHYSICIAN TO LCC HOSPITALS

AMONG the presenting symptoms for which we are most frequently consulted, a complaint of chronic fatigue is a strong competitor for pride of place Equivalents such as weakness, tiredness, weariness, exhaustion, lassitude, or lack of energy may each possess some essential distinction, but all are on the whole regarded as denoting the same sort of sensation with resentment at the inability to accomplish as much as others apparently do or as the sufferer believes he is entitled to expect

The manual worker seldom seeks advice for such a *symptom, and if he does we are justified in suspecting* some responsible serious pathological state, although, on the whole, the sufferer from organic disease rarely mentions fatigue except incidentally Traditionally, we associate asthenia with certain grave diseases or illnesses —myasthenia gravis, Addison's disease, malignant disease, diabetes, tuberculosis, profound anæmia, for example Myxœdema and the debility following certain infections, especially influenza, may be included But the majority of our patients who complain of chronic fatigue are deficient in physical signs or in the revelation of abnormalities by accessory aids to diagnosis They are annoyed with us because we find no removable cause by way of explanation, we are disappointed because we have nothing specific to treat. We agree that in present-day phraseology the psychosomatic approach is extending into medical education; but the lay belief that there is something pathological that should be removed, or that we ought to provide an essential energiser or substitute for some deficiency, receives some sympathy from the materially minded practitioner whose education has been on older conventional lines Temporary relief after operations is not surprising, whether due to the stimulation by hope and expectation or to the rest imposed after such procedures

POPULAR EXPLANATIONS

For this common disorder we can identify fashionable explanations and corresponding fashionable therapeutic cults. The oldest, and one which has never been displaced, is that of focal infection or that most specious question begging condition "auto-intoxication" For even after laborious search has failed to incriminate accessible teeth, tonsils, sinuses, appendix, gall bladder, prostate, and pelvic organs, there is the unlimited field provided by the alimentary canal The ancient joke in *Punch* of the early days of the century will be recalled—the navvy confronting his doctor with the lament, "I eat well, drink well, sleep well, but whenever there's a job of work I come over all of a tremble" "Clearly," observed Lauder Brunton, "this is an example of toxæmia from overeating"

Ingenious advertising has done much to perpetuate the belief that the cause of tiredness, or alternatively of lack of energy, can always be found in the alimentary canal, and that cure consists in either the provision of a pabulum of great restorative and stimulating value or the eradication of intestinal poisons. In my student days, "High o er the fence sailed Sunny Jim 'Force' was the food that mixed him" Later we were invited to contemplate the convincing transformation of the chronically tired into the insatiably energetic as a result of the "little daily dose" Later still, the same lesson was taught by pictorial contrasts between Mr, Mrs, or Master Can and their opposite numbers the Can ts And until restrictions in advertising space were imposed by the war, we were regularly confronted with the competing claims of a large variety of energy ensuring patent foods Some of these appealed for the elimination of what was termed 'night starvation,' the leit motif of which was that since even during sleep the energy demanded for maintenance of the vital processes may be such as to deplete the reservoirs, provision of a particular preparation on retirement to rest will convert the inadequate into a highly successful performer We who confess to ignorance of the fundamental principles of sleep may find it difficult to refute the claim

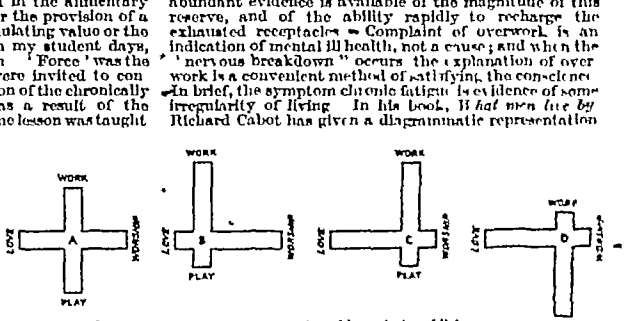
The more scientifically minded preferred to prescribe "tonics" or sedatives, according to the predilection of the prescriber Since certain endocrine dysfunctions were clearly recognisable in accepted asthenic states, corresponding organotherapeutic products had their advocates unconvinced by the assertions of laboratory workers that these were completely devoid of any activity however administered, or of any effect beyond that of pure suggestion The most modern application is that of the vitamins, whose supporters claim a great deal more than the provision of energy or the elimination of fatigue in the treatment of a multitude of conditions for which relative vitamin deficiency is regarded as responsible

When one considers the problem as psychosomatic, although the psychological side undoubtedly predominates, something has to be presented for the anatomical or metabolic influence A good example is afforded by the revelation of consequences that ensue upon lowering of the blood sugar level through the use of insulin An attractive explanation of chronic fatigue in respect to hypoglycæmia was irresistible But although the blood-sugar level has some relation to symptomatology, it is not the simple mathematical relationship that might have been expected In fact the complexity of this psychosomatic problem is well represented by the treatment recommended—the administration of "complex carbohydrates" and of atropine combined with appropriate psychotherapy—indicating that the blood-sugar level *is only an incident in imbalance of tonus of* the vegetative nervous system with its physico psychical implications

IRREGULAR LIVING

Imperfect hygiene is easily recognisable in the large majority of the intelligentsia and the professional classes generally, although it is not easy to construct a convincing indictment The man who is "out of training" through overeating, excess of alcohol and tobacco, and insufficient exercise may in some way produce or fail to eliminate some of those mysterious elusive "toxins" Or may one explain the effect as a lowering of the threshold of consciousness to physical fatigue, so that, expecting the sensation, the subject finds what he is looking for? In some instances it is evident that so much energy is wasted in unprofitable cerebral activity, in worry, in fits of temper, and in riots of emotion that insufficient remains for the serious business of life Overwork is often advanced as the explanation the sufferer implying that he is a legitimate candidate for sympathy and pity as a martyr or a hero, devoting a life of self sacrifice to the interests of others or resenting the lack of adequate appreciation of a disproportionate burden.

If work is congenial excess is hardly possible It is convenient if question begging to talk of a reserve store of nervous energy to be used only for emergencies, which even if depleted is replenished by subsequent rest And abundant evidence is available of the magnitude of this reserve, and of the ability rapidly to recharge the exhausted receptacles Complaint of overwork is an indication of mental ill health, not a cause; and when the "nervous breakdown" occurs the explanation of overwork is a convenient method of satisfying the conscience In brief, the symptom chronic fatigue is evidence of some irregularity of living In his book, *It that men live by* Richard Cabot has given a diagrammatic representation



Cabot's diagrammatic representation of irregularity of living

in the form of a cross, here reproduced, its four arms applying to the essentials, work, play, love, and worship These terms must not be too literally interpreted, a degree of liberality and some qualifications must be accepted Thus, the "work" must be psychically satisfactory, free from monotony, drudgery, anxiety, fear, gross physical insults, lack of progress or of production, the foundations of "overwork"

"Play" comprises something more than physical exertion or self-indulgence and dissipation Enjoyment which is essentially individual is a sine-qua-non and relaxation plays an important part "Love," too, will have physical and emotional repercussions as well as a sexual connotation and "worship" applies generally to all spiritual outlets and not merely to theological abstractions or church-going If A represents the perfectly balanced individual in whom the four limbs of the cross are equal and there is no disproportionate excess or deficiency, the asymmetrical variations B, C, and D are examples of candidates for "chronic fatigue" B typifies the unloved spinster and her analogies in various spheres C is "the tired business man" of the lay press, and D will correspond to a number of members of society all of whom might be comprehended as "bright young things" even if neither bright nor young

* * *

Perhaps this is over-simplification and Cabot's convenient mathematical representation of life and living may not be received with much sympathy or enthusiasm in these days when so many appear to be justly entitled to consideration as the victims of "overwork" Yet a conscientious examination of all the circumstances will lead to a fair assessment of the part actually played by the physical and mental output in the production of chronic fatigue and provide support for the opinion that "overwork" is indeed a grossly overworked explanation

DAMAGED INTERVERTEBRAL DISK

EARLY DIAGNOSIS AND TREATMENT*

E J CRISP, M B CAMB

CONSULTANT IN PHYSICAL MEDICINE, SECTOR X, EMS

ALTHOUGH sciatica does not invariably follow injury to a lumbar intervertebral disk, it does so fairly frequently, but there is almost always a latent period of weeks, months, and occasionally years before the onset of crural pain At the time of the trauma, or shortly afterwards, low back pain and tenderness to pressure over the affected segment develop but at this stage there is no pain in the leg It should be obvious that this is the correct time to diagnose the condition and to immobilise the spine so as to allow repair to take place Unfortunately in the absence of sciatic pain the true nature of the disability is seldom realised, and under the label of acute sacro-iliac or lumbosacral strain, or the still looser diagnosis of fibrositis, the case is referred to the physiotherapy department with a request for heat, massage, and exercises

For many years I have recognised a type of painful lower back, with well-marked and constant distinguishing features, which is seldom improved by physical treatment but almost always deteriorates until sciatic pain develops Previously I attributed the syndrome to referred pain secondary to sacro-iliac strain and not only watched the onset of sciatica on many occasions but accepted it as inevitable More recently I have realised that the condition is caused by injury to an intervertebral disk, and the clinical signs are so clear-cut that, once the mechanism producing them is understood, diagnosis becomes easy.

CLINICAL PICTURE

Clinically these cases are distinguished by extreme and persistent spasm of the lumbar portion of the erector spinæ muscle and hamstring spasm of less severity. When the patient stands erect, little abnormal is noted beyond a slight increase in the lumbar curve, but on his bending forward to touch the toes a remarkable degree of lumbar spasm becomes obvious (fig. 1) This is sufficient to prevent any forward flexion in the joints of the lumbar spine, there being movement only at the hip-joints and the upper dorsal region Some hyper-extension and lateral flexion, however, are usually possible

Besides these clinical signs there are characteristic symptoms The patient will complain of continuous aching lumbar pain which is aggravated by movement and coughing and often radiates into the groin There will be tenderness to deep pressure over the sacro-iliac joint and the interspinous ligament of the affected segment The sacro-iliac tenderness often develops first; this may explain diagnostic errors. Scoliosis is unusual at this stage, but, as the case gets worse, hamstring spasm increases on the affected side, and on bending forward the body inclines to the side of the lesion

Since I realised that this type of back was pathognomonic of a recently injured disk, and that continued activity might be followed by sciatic pain, all such cases referred for physiotherapy have been admitted to hospital and treated by complete rest, either in bed or a plaster-jacket. Results in the cases so treated have been extremely satisfactory The patients have lost their lumbar pain, they have not developed sciatica; and they have been discharged from hospital in 6–8 weeks with nothing worse than some residual, but permanent, stiffness of the back

PROBABLE SEQUENCE OF EVENTS AFTER INJURY TO DISK

What happens within the spinal canal after an intervertebral disk has been damaged is somewhat conjectural, but by observation of the clinical signs one can deduce the most likely chain of events with reasonable accuracy It is probable that the annulus fibrosus only sustains a minor tear at the time of the injury, and that the nucleus pulposus is not protruded until later

Directly after the injury the muscles around the affected disk and for several segments above and below go into protective spasm This is Nature's method of dealing with the lesion—an attempt to immobilise the lumbar spine in a position which will allow repair to take place and at the same time prevent further damage. The fixed lordosis which follows injury to a disk satisfies these requirements With the spine in this posture the damaged part of the annulus fibrosus is relaxed, healing thus being facilitated, and it is protected from further trauma because forward flexion is impossible. Further, the posterior borders of the vertebræ are approximated and form a barrier to protrusion of the nucleus pulposus (fig 2)

If the diagnosis is made promptly and the spine is kept immobilised in this position, the tear in the annulus fibrosus may be repaired by scar-tissue The disk is avascular and therefore unable to form granulation-tissue, but the posterior longitudinal ligament, which is usually injured at the same time, has a blood-supply, though only a sparse one. Thus damage to this ligament can be made good in the usual way by scar-tissue, and it is reasonable to suppose that blood-vessels from it may canalise the tear in the annulus fibrosus, in much the same way that blood-vessels from the conjunctiva grow across the cornea in certain types of corneal ulcer

The resulting scar-tissue will not allow the disk to regain its former elasticity, and, to prevent further injury, adaptive shortening of the muscles and ligaments in its neighbourhood takes place Consequently a portion of the lumbar spine remains permanently lordotic (fig. 3), and what might be termed a fibrous ankylosis protects the healed disk from further injury

If the diagnosis is not made at this stage and the patient is allowed to remain ambulatory, normal healing may be prevented. In consequence of hydrostatic pressure from within and torsional strain from without, the tear in the annulus will gradually increase, with correspondingly increased symptoms and the probable onset of root-pain Finally the fibrocartilage may rupture completely and allow the nucleus to herniate When this takes place the lumbar spine becomes flattened (fig 4) or even kyphotic (fig 5), and, though a limited amount of forward flexion now becomes possible, extension is completely prevented by the protrusion The condition is comparable with the displaced meniscus which impedes full extension of the knee-joint The protrusion may also cause lateral angulation between its

* Read to the British Orthopædic Association on June 1, 1945

Fig 1

1—Typical case of damaged intervertebral disk of two months duration showing limitation of forward flexion.

3—A "healed" disk: spine had been immobilised in plaster jacket nine months previously. Patient is now free from pain and normal range of flexion has returned except at the site of the lesion (lower lumbar vertebra).

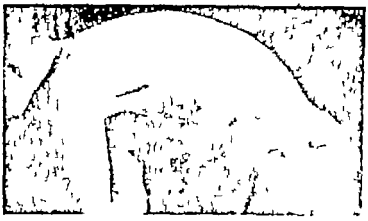


Fig 3

two adjacent vertebræ, so that the lumbar spine develops a lateral tilt, and the intervertebral space on the affected side becomes opened out laterally as well as posteriorly This is the ideal position to allow the hernia to reduce, and accordingly protective muscle spasm tries to maintain the lumbar spine in this posture. Ultimately, when the œdema has subsided, the extruded nuclear material usually slips back into the body of the disk. The lumbar spine then reverts to its normal curve, and protective spasm holds it in fixed lordosis to allow repair of the annulus fibrosus

It is not suggested that this chain of events takes place in every undiagnosed disk injury, for no doubt the damage is often slight and healing is spontaneous But it is equally certain that repair is often incomplete and not only causes intractable backache but also leads to considerable difficulty in diagnosis Patients with a lesion of this type often suffer recurrent attacks of acute lumbago indicative of further trauma and the true nature of the condition is only recognised when the disk ruptures completely

EARLY DIAGNOSIS OF INJURED DISK

Radiograms, though often diagnostic after protrusion of the nucleus, are of little value with a recently damaged disk, and their chief value lies in the exclusion of other pathological conditions *We are therefore compelled* to make the diagnosis on the history and our clinical examination

Often it will be impossible to obtain any history of recent injury to explain the symptoms, but we must not let this mislead us, for the diagnosis can be made with complete confidence on clinical grounds alone While the subjective symptoms are of considerable importance, the objective signs are of the utmost significance, the intense lumbar spasm and the "tight" lumbar spine together making an unmistakable picture.

This lumbar spasm is quite unlike anything else of its kind and the way in which it persists unchanged week after week is pathognomonic In sacro-iliac strain and fibrositis the muscle-spasm is less severe, of limited duration, and always allows some degree of forward flexion in the lumbar spine Moreover, these latter disabilities usually respond favourably to procaine injection, whereas an injured disk derives no benefit from this form of treatment

Once it is appreciated that persistent lumbar spasm and a "tight" lumbar spine in an otherwise healthy patient indicate trauma to a disk, most cases should be recognised and dealt with before the onset of sciatic pain. Certain other conditions affecting the lumbar spine—such as spondylolisthesis, Schmorl's nodes, osteochondritis, ankylosing spondylitis, and tubercle—may produce a similar picture, but they can all be excluded by careful clinical and radiographical examination In all these conditions one or more intervertebral disks are involved, so it is not surprising to find this characteristic protective muscle-spasm

REASONS FOR FAILURE TO MAKE EARLY DIAGNOSIS

Various reasons can be advanced for failure to diagnose the injury at the first onset of symptoms. The chief reason is that, although we have accepted herniation of the nucleus pulposus as a common cause of sciatic pain, we have not yet learnt to think of the damaged disk as a separate entity and, when faced with a case of this type, *are apt to mutter "It looks like a disk, but* it can't be the patient hasn't got sciatica'

The word fibrositis, used today as a label for every *ache and pain of doubtful origin, is responsible for many* mistakes Textbooks on medicine give up few pages to the subject, and we likewise should limit our use of the term It cannot be too strongly emphasised that muscle-spasm is not fibrositis, though it may lead to it The spasm met with in lesions of the intervertebral

Fig 2

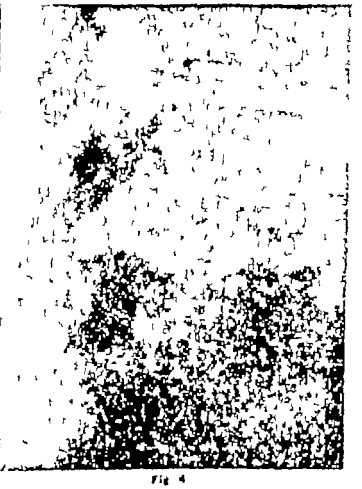


Fig 4

2—Injury to disk between L4 and L5 Note lordosis and approximation of posterior borders of bodies of L4 and L5

4—Flattened or "reversed" lumbar curve after protrusion of nucleus intervertebral spaces being opened up posteriorly

disk protects the injured disk from further trauma in exactly the same way that the rigid abdominal wall guards the inflamed appendix—it may be said to represent the orthopædic surgeon's acute abdomen

The belief that severe trauma is necessary to rupture the annulus fibrosus is another popular misconception In a recent series the injury was often trivial, and often no history was obtainable

Four members of the NFS had symptoms typical of a damaged disk, but none of them could recollect any accident Firemen often jump from a considerable height, and an awkward landing might well cause a slight split in the fibrocartilage, which though symptomless at the time would be aggravated by subsequent activity

A young lady with six months' history of low backache coughed violently while smoking a cigarette and protruded a nucleus spontaneously

Two primiparæ in their early twenties developed low backache a fortnight after parturition, one felt a click

Fig 5—Typical lumbar kyphosis after protrusion of nucleus

Fig 6—Plaster-jacket applied in a case of damaged intervertebral disk

in her back while doing postnatal exercises, the other was unable to account for her pain, both in due course developed characteristic sciatic pain This suggests that the physiological relaxation during the later months of pregnancy may render the lumbar intervertebral disks especially vulnerable

TREATMENT BY CONSERVATIVE METHODS

Once the implications of the various abnormalities of posture which may develop after injury to an intervertebral disk are appreciated, treatment becomes possible on a rational basis, and we can relieve most patients by conservative methods

Nature tries to immobilise the lumbar spine in the optimal position for the patient's comfort and for repair In this she only partly succeeds, for during sleep there is some relaxation of the muscle-spasm, which permits movement in the damaged segment and aggravates the symptoms—in fact, the nucleus is sometimes actually protruded during the night We accordingly immobilise the spine in a plaster-jacket Two cardinal rules must be observed if success is to be achieved: first, in applying the jacket no attempt must be made to correct the deformity, for experience shows that this only leads to increased pain, secondly, the plaster must be worn long enough for the torn disk to become soundly healed Immobilisation for 6–8 weeks appears to be sufficient for the partially ruptured disk diagnosed shortly after the injury and without sciatic symptoms The plaster should be applied with the patient standing in the position of greatest comfort (fig 6)

When the condition is only diagnosed after the onset of crural pain, a longer period of immobilisation obviously becomes necessary, for the damage and reaction will be more extensive. Usually the condition is recognised while the rupture is still incomplete and before protrusion has taken place, the lumbar spine being in fixed lordosis, but in view of the added complication the jacket must be worn for at least three months

The completely ruptured annulus fibrosus with protruded nucleus can be treated on the same lines, but in two stages The first plaster is applied with the lumbar spine in kyphosis, and the patient remains in bed for a month or so At the end of this time the jacket is removed. The herniation will usually be found to have been reduced and the lumbar spine to have regained its normal shape A second plaster is then applied with the lumbar spine in lordosis and worn 10–12 weeks. Some patients may be unable to tolerate the first plaster and will require nursing on a plaster-bed or a bed with fracture-boards until the protrusion is reduced

Surgical treatment may be reserved for cases where the protrusion has not been reduced after a reasonable period of immobilisation, say, up to three months; also for recurrent protrusions, and for patients who still complain of severe pain long after the lumbar spine has reverted to its normal curve. In this last class the herniated nucleus has probably become fragmented, and the detached portion may be found lying loose in the thecal canal

Physiotherapy has been left until last, because its usefulness is distinctly limited The whole object of our treatment is to ensure a fibrous ankylosis round the damaged disk, and exercises to mobilise the lumbar spine or to correct errors of posture are therefore contraindicated Leg, arm, and shoulder exercises may be permitted after removal of the plaster, but the lumbar spine should be left to work out its own salvation and subconsciously increase its range of movement.

SUMMARY

The lumbar intervertebral disks suffer trauma far more often than is generally appreciated, but in the absence of crural pain or radiographic changes the resulting lesion is often mistaken for sacro-iliac strain or fibrositis

The condition may easily be recognised by the extreme and persistent lumbar spasm and the "tight" lumbar spine Early diagnosis and treatment by immobilisation should considerably reduce the incidence of sciatica.

Cases which escape diagnosis until after the onset of sciatic pain may be divided into two groups, depending on whether the annulus fibrosus is partially or completely ruptured The former group may be recognised by the fixed lumbar lordosis, the latter by the fixed lumbar kyphosis. Both groups usually respond well to immobilisation in a spinal jacket.

PROTRUSION OF INTERVERTEBRAL DISK

B H BURNS
M B CAMB, F R C S

R H. YOUNG
M B CAMB, F R C S

SURGEONS TO BOTLEY'S PARK WAR HOSPITAL

IT is widely realised that protrusion of an intervertebral disk is the commonest cause of sciatica, but what is not so well recognised is that these lesions are a common cause of low back pain In fact, it is unusual for sciatica to be the first symptom of protrusion of a disk, for attacks of pain in the low back or buttock commonly precede the sciatica for a considerable time Moreover, in our experience a protrusion of a disk is the chief cause of recurrent low back pain

Therefore, we regard what we may call the orthopædic signs as being of the greatest importance in the diagnosis of this condition Not only is it possible to diagnose a protrusion of the disk on the orthopædic signs alone, but in the early stages these are usually the only signs to be found In many instances, neurological signs may only make their appearance months or occasionally years after the onset of symptoms

This paper seeks to emphasise the importance of lesions of the disk in low back pain and sciatica. It is based on the records of 604 inpatients suffering from these complaints treated at Botley's Park between 1940 and 1945, including 141 cases of disk lesions proved at operation

HISTORY AND SYMPTOMS

The diagnosis of a protrusion of a disk depends on the history, back signs, and the sciatic nerve tension (head and knee) test We have come to regard neurological signs as merely confirmatory and an indication of the severity or duration of the lesion

Of 141 patients in whom we have found lesions of the disk at operation, 104 have been males and 37 females; 70 had had an injury of the sort that might damage the disk, and 62 recalled no such injury A few of the latter, particularly those in the Services, have been undertaking heavy work at the time of the onset of their symptoms, but being at the same time exposed to wet and cold have attributed their pain to this more popular cause

The type of injury or work associated with the majority has been *heavy lifting* and *falls on the buttocks*, which include heavy landings in an aeroplane and tank driving over uneven country

Of the 141 patients, 109 have had one or more attacks of lumbago before the onset of sciatica A proportion of them have had repeated attacks over many years, the longest history of recurrent backache being 28 years In only 21 cases did the trouble commence with pain in the leg and in 11 others with pain in back and leg simultaneously

The attacks of backache in the early stages commonly last 1–2 weeks to 3–4 months, or longer In the interval between attacks many are free from pain and have a full range of movement Others are never quite free from symptoms, suffering always from a lame back with some pain and restriction of movement After a time the pain may spread down the leg This may occur gradually, or suddenly with an acute attack of sciatica In a few the pain may leave the back and thereafter the patient may suffer from sciatica only Pain is often absent at rest and only brought on by exercise, standing for more than a short period, or sitting A particularly common feature is that the patient dislikes sitting for more than a short time—e g, he is unable to sit through a cinema programme in comfort He often finds relief from a pillow in the small of the back

Pain on coughing or sneezing is a frequent complaint, and paræsthesia of the foot and toes is usual in the severer cases

SIGNS

About half of our patients with proved disk lesions have had no deformity of the back on standing Of those that have a deformity most have only a slight list or inclination to one side Some have loss of the lumbar hollow and a few have a well marked sciatic scoliosis Incidentally, it may be said that almost the only cause of sciatic scoliosis is protrusion of a disk

The most notable and constant characteristic of a disk protrusion is restriction of movement in the antero-posterior plane while sideways bending is free In the most severe attacks sideways bending is largely maintained; even in sciatic scoliosis it is surprisingly full in the direction that increases the deformity On bending forwards a tilt or inclination to one side often occurs even though it has not been present on standing In others there is no tilt on bending forward, but this movement is restricted Extension is sometimes limited, particularly in those with loss of the lumbar hollow

Tension test—The straight leg raising test (Lasegue's sign) is of limited value in the diagnosis of disk lesions Certainly, except between attacks it is positive—i e, the movement is restricted and painful—but so it is in some other conditions To make the test more precise, it has been elaborated by one of us

The affected leg is gradually raised with the knee straight until pain is felt The knee is then flexed, but only just enough to relieve the pain When tension on the hamstrings is released by flexing the knee, the pain will only persist if it arises in the hip-joint In all other conditions, both intraspinal lesions, and extraspinal lesions such as gluteal fibrositis and sacro iliac strain pain will be relieved

Intra and extra-spinal lesions of the low back may now be distinguished by continuing the test as follows:

With the leg raised and the knee flexed just sufficiently to relieve the pain the head is flexed on the chest; the pain if due to intraspinal lesions or lesions of the erector spinæ muscle or its fascia, will return Further flexion of the knee will release the tension on the meninges and consequently the pain from an intraspinal lesion will go but relaxing the hamstrings will have no effect on the erector spinæ, and consequently in myofascial lesions the pain will remain.

Neurological signs—In severe or long-standing lesions of the disk neurological signs may be present, although even then the signs may be only slight. Among the signs that may be found are the following:

Sensation may be dulled—usually over the outer side of the foot and sole The ankle jerk may be diminished or absent but occasionally it may recover between attacks The knee jerk is very rarely affected Muscle wasting and loss of tone may occasionally be pronounced especially in the calf sometimes in the buttock, thigh, or anterior compartment of the leg Muscle weakness, tested by the ordinary methods, is uncommon but it may be noticeable in the extensors of the toes and in the dorsiflexors of the foot

It is perhaps possible to relate the symptoms to the stages of the lesion The initial attacks of lumbago with lumbar spasm are probably due to the gradual bulging back of the protrusion causing tension on the posterior longitudinal ligament, which, as shown by Roofe (1910) and confirmed by ourselves, is liberally supplied with nerve-fibres Sciatic pain, however, is not felt until the protrusion becomes large enough to irritate the nerve-root Neurological signs will not appear until later, when intraneural changes such as œdema, ischæmia, or fibrosis have occurred

DIFFERENTIAL DIAGNOSIS

There are few conditions that give a similar clinical picture to that of a disk lesion In spondylolisthesis it sometimes happens that the nerve-root becomes adherent to the ledge made by the back of the body of the vertebra below The condition may then be indistinguishable clinically from that caused by a disk lesion X ray films must therefore be scrutinised with the greatest care, for a small apparent slipping may be the cause of a very palpable ledge

In spondylitis—a not uncommon cause of pain in the young adult—and in other forms of arthritis there is restriction of lateral bending, and the presence of these conditions can usually be confirmed by radiography

Sacro-iliac arthritis may occasionally be difficult to distinguish but the head and knee test, which is negative will serve to differentiate it, and confirmation may often be obtained by the pain produced on attempting to compress or distract the iliac crests The Trendelenburg test may also be positive

The frequency of neoplasms as the cause of low back pain and sciatica has probably been exaggerated, and in the record of 1000 cases of backache kept by one of us (R.H Y) only 6 were due to secondary carcinoma

Variations in structure of the lower part of the back—and there are many, such as sacralised 5th transverse process, anomalies of the facets, &c—were often thought to be the cause of low back pain and sciatica It is possible that these conditions may be the source of irritation of nerve-roots, but the evidence is not convincing

In many visceral lesions, including particularly gynæcological and renal conditions, pain may be referred to the back, but in them movements of the spine are not restricted

There remain a number of ill-defined lesions of doubtful frequency—among them displacement or strain of the sacro-iliac joints, myofascial lesions, and fibrositis. These diagnoses may be made in acute or single attacks but when the trouble is persistent or recurrent a lesion of the disk is more likely It may be said that the picture that used to be ascribed to sacro-iliac strain is that which we have now come to associate with lesions of the disk. In myofascial lesions and fibrositis, not in our opinion common causes of recurrent backache, the tension test is negative and lateral bending may not be free

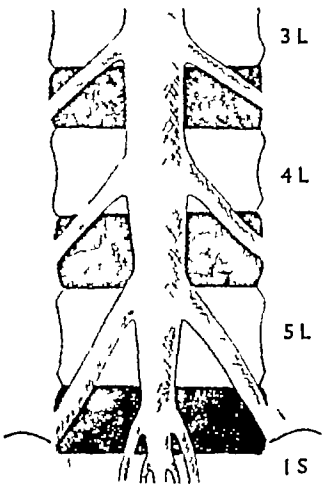
CONSERVATIVE TREATMENT

With increased experience we diagnose disk lesions more often than we used to, and our threshold for operation is lower However, we find it necessary to

operate on only about 2 out of every 5 patients diagnosed as having a disk lesion. When the symptoms are slight and have never been severe we recommend the patient to wear a belt or corset to restrict the movement of the lumbar spine

If the patient is seen in a first attack he is put to bed to rest and relieve the lumbar spine from strain. We have found that where rest is likely to be successful the symptoms rapidly improve, and in about half the cases it may be expected that the attack will subside If after about three weeks there has been no improvement operation is recommended, for rest is unlikely to result in permanent cure and delay causes unnecessary suffering and possibly a neurosis.

It used to be our practice to persist with rest and immobilisation in a plaster bed for many weeks. This often failed to give relief, and is, in our present opinion, a less acceptable procedure than operation We have not favoured the use of a plaster jacket, for it has seemed to us a much less comfortable and no more effective means of immobilisation than a corset. Heat, massage, electrotherapy, and injections of procaine may give temporary benefit in an attack by relieving spasm, but their effect, if any, is only transitory



Relation of the lumbar nerve-roots to the intervertebral disks (black)

(From a photograph of a dissection.)

The need for operation is clear in the more severe cases, but the decision to operate in the less severe ones will be influenced by many factors On the one hand, operation is safe, and offers a high prospect of complete and lasting relief None of our patients has been made worse by laminectomy, and in no instance has a back been noticeably weakened On the other hand, operation necessitates three weeks in bed and a month of rehabilitation Thus, the choice between operation and conservative treatment depends on balancing the amount of pain and disability against the inconvenience of, and the time spent recovering from, the operation

It must also be borne in mind that too long a postponement may make the operation more difficult and less likely of success, for adhesions may become dense around the nerve-root and even the dura. There may also be damage to the anterior root, recovery from which may be long delayed

LOCALISATION

When operation has been decided on, accurate localisation of the lesion is desirable but unfortunately it is not possible because X-ray films, either plain or with contrast media, and neurological signs are of very little help However, the great majority of protrusions come from the disks between the 4th and 5th lumbar vertebræ or the 5th lumbar and 1st sacral (92% according to Love 1939), and some 6% come from the disk between the 3rd and 4th lumbar vertebræ

X-ray films have shown diminution of the space between adjacent vertebræ only in old lesions and then it is often accompanied by osteo-arthritic lipping The use of contrast media and pneumograms has been generally given up, for not only do these methods fail to show laterally placed protrusions, but at times they are actually misleading We have had two instances of a radiogram indicating a protrusion of the 3rd/4th lumbar disk when the actual lesion disclosed at operation was in the disk between the 5th lumbar and 1st sacral vertebræ Incidentally, it may be mentioned that on opening the meninges to let out the 'Lipiodol,' a considerable degree of arachnoiditis was often observed.

Neurological signs often fail to localise the lesion This is to be expected on account of the anatomy of the [illegible] and the varying position of the protrusions From a dissected specimen it can be seen that the relation of the nerve-roots to the disk varies at different levels of the lumbar spine In the lower lumbar region the nerve-roots issue closer together and pursue a nearly vertical course; thus a large protrusion of the disk between the 5th lumbar and 1st sacral vertebræ may easily press on two roots A similar arrangement is seen at the 4th/5th lumbar disk. We have observed this at operation on more than one occasion when we have seen two nerve-roots adherent to one protrusion

Further, the nerve-root affected depends to some extent on whether the protrusion is laterally or medially placed, a lateral protrusion is likely to involve the upper nerve-root and a medially placed one tends to press on the lower root. Also the protrusion may occur at the upper or lower part of the disk and spread upwards or downwards over the adjacent body

The difficulty in localisation by neurological signs is illustrated by the following two cases In one a large protrusion was found at 5/1 disk, when, from the area of anæsthesia and the presence of anterior crural pain, we had diagnosed it at the level of the 3/4 disk. In the other the lesion was thought to be at 5/1 when it was actually found at 3/4

OPERATION

We use a free exposure because it gives easier access and a more comprehensive view of the pathology than the small interligamentous approach or a hemi-laminectomy The 5th lumbar and adjacent parts of the 4th lumbar and 1st sacral spinous processes are removed The dura is then exposed by removing the 5th lamina and adjacent ligamentum subflavum The dura is not opened and care is taken to avoid damage to the lateral vertebral joints

Large protrusions are plain to see but smaller ones are not so easily recognised On incising the capsule, disk substance often begins to extrude and in some instances it is found to be completely free and easy to pick out in its entirety. In this case it is probably the expelled nucleus pulposus. On other occasions the material is firmly attached inside the disk. It is then likely to be a loose piece of torn annulus

This last type of disk protrusion—ball-valve type—is apt to swing in and out in a manner similar to a torn cartilage of the knee, and unless all the torn part is removed it may be the cause of a recurrence of the symptoms. If the operation is undertaken when the displacement is reduced it is not so easy to detect the presence of the lesion. Therefore it is easier to do the operation during an attack. That an abnormality is present even in the absence of a well-marked protrusion may be detected from the consistency of a part of the disk. It is soft and springy and its surface is irregular, unlike the rest of the annulus

In long-standing cases the protrusion may be adherent to the nerve-root or theca and freeing the adhesions in order to get access to the disk may be troublesome

Occasionally no disk protrusion is found but an osteophytic lip of the posterior part of the body, or a ledge from an undetected minor degree of spondylolisthesis, may be discovered. To these projections nerve-roots become equally adherent so they should be freed and if possible the projection should be bevelled off There is apparently no disadvantage in performing a laminectomy on cases of spondylolisthesis The affected spinous process is nearly always loose and can play no part in the stability of the back

After-treatment—Patients move around from the start, and on the 2nd or 3rd day, by which time they can easily roll over on their face, extension exercises are commenced Flexion exercises are begun on the 14th day Patients get up on the 21st day and gradually increase their activities Many of them feel the need for a support for a time and our practice has been as a rule to fit them with a belt The great majority have had a full range of painless movement within 2 months but it has seemed to us unwise to allow them to lift heavy weights until 9 months has elapsed

RESULTS

In our earlier cases we attempted accurate localisation by myelography and neurological signs We consequently limited the scope of the operation to the site

indicated by the findings. As previously stated, these methods were misleading, and consequently we sometimes failed to find a protrusion—in fact, out of the first 60 cases, in 10 no disk protrusion was discovered. Although none of them is worse, except one from a lipiodol arachnoiditis, some of them are no better.

Since our operation became virtually an exploratory laminectomy, and we have not attempted accurate localisation or relied on neurological signs, we have found the lesion in a greater proportion. Of the last 112 cases, we have found a protrusion of a disk in 93. In the 19 patients in whom no disk lesion was found, the following pathology was discovered:

Osteophyte with adherent nerve root	7 cases
Spondylolisthesis with adherent nerve root	8 "
Peridural adhesions	2 "
Pathology not clear	2 "

We have examined our results in the two types of disk lesion. Of 62 protrusions of the nucleus pulposus (disk material lying completely sequestrated), 61 were immediately relieved. Only 1 has had a recurrence since. Of 70 annular tears (disk tissue attached), 70 were immediately relieved, 8 have had recurrent attacks since, and 1 was not relieved of chronic pain.

Some of the 9 poor results in annular tears were probably due to the fact that, because we did not appreciate the extent of the torn tissue, it was incompletely removed.

DISCUSSION

Most of our patients had suffered from pain in the back before the onset of sciatica. During that time they had been diagnosed as having sacro-iliac strain or a myofascial lesion, usually fibrositis. Even after the onset of sciatica the diagnosis of protrusion of a disk was rarely made, and that of a myofascial lesion was retained. The work of Kellgren seems at first sight to support this attitude. He found that when hypertonic salt solution was injected there was referred pain, which was relieved by subsequent injection of procaine. But Weddell, Feinstein, and Pattle (1944) using electromyography, have shown that local spasm may be the effect of a central cause—e.g., an irritated nerve-root.

Myofascial lesions may be the cause of an acute or a chronic attack, but it is not easy to see how they can be responsible for recurrent attacks. Such lesions are not accused of it in other parts of the body. For instance, the pain from a tear of the extensor tendons of the forearm (tennis elbow), once cured, does not recur. Nor does the pain arising from a sprain of the internal lateral ligament of the knee recur; when a young adult has recurrent attacks of pain and disability in the knee, the cause is, almost without exception, an internal derangement. Similarly, recurrent attacks of pain in the back between the age of 20 and 40 are also likely to be, so to speak, an internal derangement—a disk lesion.

The more experience one has of intraspinal pathology, the less readily does one accept the diagnosis of sprains, strains, and rheumatism in chronic or recurrent backache. Looking back on our records there are many patients in whom we made these diagnoses and whom today we should confidently take to be suffering from a lesion of the disk, and be virtually certain of finding one at operation.

SUMMARY

Recurrent backache in young adults is most often due to protrusion of an intervertebral disk.

The earliest manifestation is backache, not sciatica.

The history and clinical findings are the most reliable guides in diagnosis. Precise localisation can be achieved only by laminectomy. Myelography and neurological signs are of no help in localisation.

In 177 laminectomies performed for suspected lesions of the disk, protrusions were found in 141. In 19 of the others intraspinal abnormalities to which there was good reason to attribute the symptoms were found.

Of the 141 with proved disk lesions 131 were immediately relieved and have remained free of symptoms to date.

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LUMBAGO

MECHANISM OF DURAL PAIN

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For centuries lumbago has been regarded as a rheumatic manifestation. More recently "myalgic spots," "trigger areas," and fat hernias in the muscles have been given aetiological significance. It is evident that abnormalities have been sought in the lumbar muscles without critical inquiry into whether or not lumbago is primarily a muscular lesion. In my view it is not; it is the result of an attack of internal derangement of a low lumbar joint. This is an unorthodox assertion but the fact that lumbago is an intraspinal lesion can be simply corroborated by any doctor who cares to induce epidural local anaesthesia in a series of cases. Indeed, it would be surprising, if, of all the joints containing menisci, the spinal were alone in immunity from attacks of internal derangement. These cases are usually labelled "lumbar fibrositis," but I am sceptical of the existence of such a disorder in the sense of widespread affection of both sacrospinalis muscles or lumbar fascia; at any rate no such case was discovered among the last 500 cases of backache seen by me. In my experience fibrositis in the lumbar region occurs unilaterally as one isolated area of scarring.

Lumbago may be defined as lumbar pain of sudden onset, severe enough to immobilise the patient for a short time. The usual story is that the patient bends down and is seized with such violent backache that he is unable to move. He may remain flexed for a few seconds and then slowly straighten up, he may have to be carried to bed and stay there motionless for several weeks. The pain is usually equal on the two sides of the back, occasionally it is asymmetrical; strictly unilateral pain is uncommon.

THREE STAGES OF DISK SYMPTOMS

Abnormality of a low lumbar intervertebral disk shows itself in three ways: as backache, as lumbago, and as sciatica. The lesion is the same in each case; the amplitude, direction, and suddenness of the movement of the loose intra-articular piece of cartilage govern the type of pain experienced. These three symptoms by no means follow an orderly sequence. Patients may start with sciatica and, after recovery, find themselves subject to attacks of lumbago; backache may gradually progress to sciatica; attacks of lumbago may occur at intervals for years without altering in character. Many defective disks at the lower lumbar levels give rise to no symptoms. Patients in their fifties found to possess a fragmented annulus fibrosus may describe an attack of transitory sciatica in their teens and no further trouble until a recurrence was brought on by, say, a fall a few weeks before. But for that accident, the patient would obviously have remained symptom-free for life.

Backache.—Posterior defect of the annulus fibrosus may be regarded as a failure in embryonic fusion, akin to spina bifida affecting the bone. I regard the accident mentioned by some patients not as fracturing the cartilage but as making manifest a defect already in existence. A history of lumbago or sciatica in parents and siblings is often met with; occasionally all the members of a family are affected.

The history may date from childhood. At school the back may have been apt to ache and have been found weak in one way or another. Some patients state that from their earliest recollection certain postures have brought on backache. Girls seem much more liable to early symptoms than boys. During the patient's late teens or early twenties a minor strain to the back or a period of rest in bed brings on central low lumbar aching lasting a few days or weeks. Later on this symptom recurs after exercise or prolonged standing, again disappearing after a time. Such cases are often labelled postural pain. In a limited sense this is true enough, but the term obscures the actual cause of the symptoms. "Postural pain" is merely an abstract aetiological ascription; it cannot be a diagnosis. For

it does not identify the structure responsible for the symptoms In due course backache varying unaccountably in degree from day to day is experienced; it is most readily brought on by exertion involving the half-flexed position. After some years the ache becomes more or less constant, varying in intensity, and aggravated by heavy work At first the patient wakes free from symptoms each morning; later the ache on waking is such that he gets out of bed and walks about to relieve it The occurrence of sharp twinges teaches him to move warily when turning over in bed or rising from a chair He may perceive a momentary jar in the lower back on coughing or sneezing The patient is now on the verge of his first attack of lumbago

Those patients whose occupations are sedentary may continue to suffer only from backache for many years Fragmentation of the annulus fibrosus, with consequent pain resulting from interference with the dura mater, is a far commoner cause of backache than has hitherto been supposed A small degree of posterior displacement of the loose fragment occurs after the lumbar spine has been kept flexed and the dura mater is irritated by pressure exerted indirectly through the posterior capsular ligaments

Lumbago—The patient with lumbago is usually a vigorous man aged 25–50 He may have experienced premonitory symptoms of the type set out above but may also be stricken without warning Suddenly, as he bends forwards, he is immobilised in the flexed position by agonising lumbar pain The joint is locked in flexion, as happens in the same circumstances at the knee A major posterior displacement has occurred, sudden severe pressure is exerted on the dura mater Attempts at trunk-extension, by approximating the articular surfaces posteriorly, tend to squeeze the fragment yet farther backwards, this movement is thus impossible at first

Examination reveals a patient lying in bed unable to move and afraid to cough, sneeze, or even blow his nose In the more severe cases lumbar spinal deformity may be pronounced Considerable lateral deviation may be seen, occasionally a lumbar kyphosis is noted, as a rule spasm of the sacrospinalis muscles greatly limits movement at the lumbar spine The range of straight-leg raising is greatly limited Clearly, tension on the sacrospinalis muscles is not altered by straight-leg raising until an angle of about 70° is reached, the pelvis then begins to tilt and the lumbar spine to flex The head-and-knee test for the sheath of the sciatic nerve-roots described by Cyriax (1942) is usually positive

Deformity at the lumbar spine maintained by muscular spasm results from an articular, not primarily muscular, disorder (When the knee-joint is suddenly locked in flexion even though it is spasm of the hamstrings that maintains the deformity, the condition is never ascribed to primary spasm of the hamstrings but to internal derangement of the joint) Moreover, coughing is agonisingly painful—a well-attested sign of intraspinal lesions

These findings combine to show that lumbago cannot result from a muscular disorder, for the physical signs are not muscular but partly articular and partly those well-known to result from dural irritation For this reason, epidural local anæsthesia was tried in an attempt to discover whether it could thus be proved that the lesion was intraspinal and the pain due to pressure on the dura mater In four-fifths of all cases the pain disappeared there and then None of the solution introduced could have infiltrated the lumbar muscles In the remaining (unsuccessful) cases I do not consider that the lesion was extraspinal, but that mechanical factors prevented the solution from reaching the right spot Colour was lent to this supposition by one patient's pain, epidural local anæsthesia abolished it during the first but not the second of two attacks of lumbago

Examination during the stage of recovery shows a patient with a symmetrical posture, able to bend guardedly. He moves his trunk all in one piece, often putting his hands on his knees as he rises out of a chair Asked to bend forwards, he does so maintaining his lumbar lordosis Full flexion may gradually be achieved, often after several false starts. Side-flexion is usually full and painless Extension is markedly limited by pain and apprehension; this is the last movement to become full Between attacks, examination of patients liable to lumbago reveals nothing abnormal, except when a click, often painless, can be felt as the lumbar spine moves.

Recovery is usually full after each attack; it may take from two to six weeks Patients are apt to get an attack a year, often at the same season each year. This fact has lent colour to the rheumatic hypothesis, the weather being blamed. A more probable attribution is to the activities dictated by the different seasons. The two periods of greatest incidence of lumbago were found to be summer, when holiday expeditions are at their height, and late autumn, when a great deal of digging in the garden is begun Between the ages of 50 and 60 these attacks often cease At this time the spine stiffens somewhat and the activities leading to lumbago are apt to be dropped

Sciatica is seldom the initial symptom As a rule the patient states that, as one of the now-familiar attacks of pain in the lower back was passing off, pain in the lower limb appeared as the lumbago abated This alternation of pain, the proximal symptoms disappearing when the distal symptoms come on, is characteristic of disorders of the sheath of spinal nerve-roots and is also described by patients with cervical periradiculitis ("brachial neuritis") and third-lumbar periradiculitis ("anterior crural neuritis") The mechanism appears to be that when the fragment of fibrocartilage passes laterally far enough to impinge on the sheath of the nerve-root it ceases to press on the dura mater It is open to argument whether in lumbago the annulus fibrosus is already fragmented, or whether the posterior limbs, by reason of lack of fusion centrally, are merely hypermobile Findings at operation on cases of sciatica, however, prove that at this stage one or several pieces have become detached from the main body of the defective fibrocartilaginous ring

Once sciatica appears, the characteristic signs of disk-protrusion soon become obvious, the commonest are lumbar scoliosis without rotation, limitation of straight-leg raising, and fifth-root paresis

Radiography—As might be expected in a lesion affecting fibrocartilage, no relevant abnormality is found Spina bifida is so common in normal people—Brailsford (1934) says 6%—that it is difficult to assess its importance, but the presence of one congenital abnormality makes the existence of another the more probable. Sacralisation of the fifth lumbar vertebra suggests that excessive stabilisation of the lumbosacral joint has increased the stresses on the fourth lumbar joint, where three-fifths of defective disks are found Obviously, bony abnormalities of this type do not of themselves cause symptoms

TREATMENT OF LUMBAGO

Prophylaxis—Patients liable to lumbago must avoid heavy work involving trunk-flexion They must learn to kneel and squat instead of bending forwards It is a curious fact that the most uncomfortable stance for a patient with a fragmented disk causing backache is the half-flexed position, whereas it is full flexion that encourages the onset of lumbago Obviously, in full flexion the back of the intervertebral joint gapes the most widely, and posterior displacement of the loose fragment is encouraged Should a patient liable to attacks of lumbago feel discomfort in his back lasting more than an hour, he should go and lie down at once, for it is better to spend some hours recumbent several times a year than a month off work with lumbago Attempts to "work it off" actively are usually disastrous, since they naturally bring about further displacement Recurrence of attacks at short intervals, especially in youngish patients, points to the danger of the development of sciatica from disk-protrusion Hence patients in this state should adopt lighter work, and wear a belt stiff and tight enough to limit movement at the lower lumbar spine

If the views set out in this paper gain acceptance, it will become reasonable for medical officers attached to factories to warn employers of the danger of allowing anyone with a defective low lumbar intervertebral disk to do heavy work, especially if it involves stooping, for it would be open to the workman to maintain that the final movement of the fragment that caused lumbago

or sciatica was an industrial accident Acceptance of a rheumatic causation has protected employers in the past

The usual position for nursing patients in bed is responsible for a great deal of subsequent backache Many patients found later to be suffering from defect of the annulus fibrosus report that their first bout of backache followed a period of rest in bed after an operation or a confinement The half-lying position is the greatest culprit in this respect; for it involves the maintenance of a marked degree of lumbar kyphosis. Hence patients should be encouraged to keep some degree of lumbar lordosis by lying with only one pillow or sitting upright Lying face-downwards and prone-lying extension exercises are of the greatest value in prophylaxis

Treatment of acute lumbago—The remarkable feature about lumbago is the fact that the precipitating cause and the subsequent lasting pain have separate mechanisms. Part of the defective annulus fibrosus moves backwards suddenly; this causes an internal derangement of the joint and a localised jarring of the dura mater The major part of the symptoms might thus be reasonably supposed to originate from consequent traumatic arthritis at the affected joint, but the result of epidural local anæsthesia proves that this is not so The intra-articular displacement appears momentary, and the prolonged symptoms that follow are due wholly to the very slow post-traumatic recovery of so sensitive a membrane as the dura mater Obviously, epidural local anæsthesia would have no effect on pain due to persistent subluxation within the joint nor to traumatic arthritis as such

Rest in bed.—This is the traditional treatment and is nearly always called for in the first place since immobilisation prevents any further jarring of the dura mater At this stage any movement at the lower spinal joints alters tension on the bruised area of membrane hence all movements of the trunk even flexion of the neck are extremely painful Coughing jolts the dura mater by setting up a wave of pressure in the cerebrospinal fluid and should be controlled by an effective linctus The patient should remain in bed for some days, getting up and about cautiously when he finds he can He must avoid such movements as cause pain, especially those involving trunk flexion. If he is still bedridden after some days, local anæsthesia is indicated

Epidural local anæsthesia—The injection may be given at any time if the pain is severe, but it is seldom lastingly effective during the first two days it affords up to two hours' relief, during which time the patient can move about as he likes, get comfortable, and fall asleep As a rule it possesses greater therapeutic value in cases of some days' standing The immediate local anæsthesia of the bruised area of dura mater enables the patient to move his lumbar joints, and it seems that the hydraulic effect of raising the dura mater from the posterior capsular ligaments reduces contact between the two structures and explains the lasting relief

The technique is as follows. The patient lies prone, and the cornua of the sacrum are identified The skin between them is anæsthetised with not more than 1 c.cm. of a 0·2% solution of procaine Too much solution introduced here obscures the landmarks A lumbar puncture needle is inserted into the sacral hiatus and passed to a depth of 3 in The stylet is withdrawn and care taken to see that neither blood nor cerebrospinal fluid escapes A 50-c cm syringe full of 0 5% procaine in normal saline solution is attached to the needle Aspiration is attempted, to make sure again that the tip of the needle has not pierced a blood vessel or the theca If all is well, the contents are slowly injected over a period of 5–10 min Most patients feel dizzy for a few minutes, then rise and with few exceptions find that they can move freely in every direction Two hours later the pain returns but by the next day considerable improvement is noted A well timed epidural injection usually halves the period taken to get well from lumbago

Manipulation of lumbar spine—General anæsthesia is to be avoided; for too much is done, and the dura is apt to be bruised again Under epidural local anæsthesia the patient can actively achieve a full range of movement in every direction Gentle passive movements without anæsthesia are often beneficial after the first few days since they start the joint moving again they provide the best treatment if local anæsthesia is unavailable This fact explains many of bone-setters' successes; effective treatment is given though it is based on a false concept of the nature of the disorder present

Local anæsthesia of the sacrospinalis muscles—This was the method I used when still under the impression that lumbago was primarily a muscular affection The entire extent of the sacrospinalis muscles was infiltrated on each side; this required 60–80 c cm. of solution injected into each muscle, whereupon the patient stood up and moved about. Some good results were obtained, but it is clear now that the injections merely so relaxed these muscles that an amount of movement at the affected joint was permitted which spasm would otherwise have prevented

Deep massage—Deep friction given to the lumbar muscles may also have the effect of diminishing spasm and thus increasing the range of active movement subsequently

SUMMARY

Lumbago is initiated by an attack of internal derangement at a low lumbar intervertebral joint, as the result of a momentary posterior displacement of a movable piece of intra articular fibrocartilage The prolonged subsequent pain appears to be caused entirely by bruising of the dura mater Lumbago provides the stage of symptoms due to a hypermobile or fragmented annulus fibrosus that is intermediate in degree between backache and sciatica Defect of the fibrocartilaginous ring leading to pressure exerted via the posterior capsular ligaments on the dura mater is a common, but hitherto unrecognised, cause of backache

The best treatment for lumbago appears to be a few days' rest in bed followed if symptoms persist, by epidural local anæsthesia Prophylaxis consists in the maintenance of the lumbar lordosis Radical cure—i e removal of the hypermobile or loose part of the annulus—presents such technical difficulties that it has not yet been attempted until the stage of sciatica from root pressure has been reached

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ACUTE PHLEGMONOUS GASTRITIS

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This very rare condition was first described by Varandæus (1620), who recorded a case of the localised variety, and the first case of the diffuse inflammation was recorded by Andral in 1839 The literature on the subject has been ably reviewed by Sundberg (1910), 215 cases, Gerster (1927), 203 cases; Watson (1932), 277 cases; and Ellason and Murray Wright (1939)

Two types are recognised, the diffuse and the localised In diffuse phlegmonous gastritis the condition extends from the pyloric ring for a variable distance up towards the cardia. It never extends beyond the pyloric ring, a limitation probably connected with the direction of flow and distribution of the lymphatic vessels in the stomach wall The wall of the stomach is greatly thickened with inflammatory exudates, and the inflammation usually spreads through the overlying peritoneum to give a peritonitis spreading from the stomach The mucosa of the stomach is intact; or, if it is ulcerated, the ulcer is primary—either an acute or chronic peptic ulcer or a carcinomatous ulcer through which the inflammation reaches the stomach wall Where the mucosa is intact, the inflammation is blood borne In the localised type there is a circumscribed area of inflammation of the stomach wall primarily located in the submucous tissue and often going on to abscess formation

The symptoms and signs are those of toxæmia and peritonitis. The more acute cases present the picture of a fulminating toxæmia while the milder show the signs of an upper abdominal inflammation. The disease has not been definitely diagnosed before operation As the commonest type of organism responsible is the streptococcus, the most hopeful line of treatment appears to be the administration of adequate doses of sulphanilamide When the condition is recognised at operation it is best left alone, although Weinstein and Klein (1927) advocate temporary exteriorisation of the stomach on a glass rod, advice also given by Hamilton Bailey (1944)

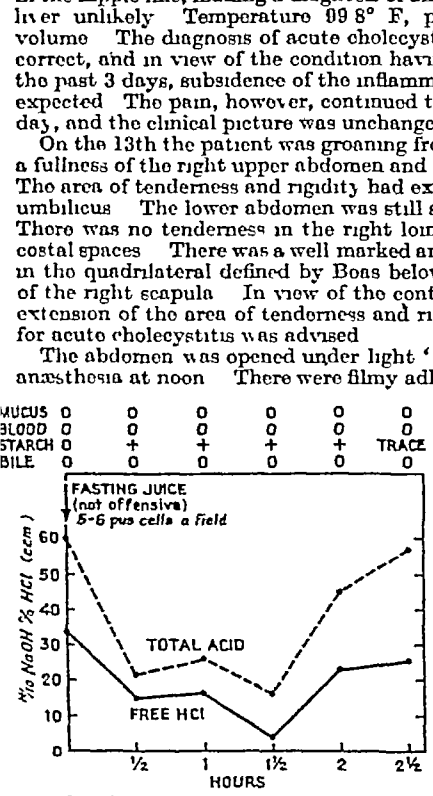
CASE-RECORD

A man, aged 60, married, Sinhalese, was admitted to the General Hospital, Colombo, on Feb 11, 1943, complaining of severe abdominal pain He had been examined by Dr Frank Gunesekara, who had advised his admission to hospital with the provisional diagnosis of acute cholecystitis The illness had begun 3 days previously, while the patient was at dinner, with an acute pain starting in the left upper abdomen, soon becoming a diffuse upper abdominal pain The patient had no sleep that night, and had vomited fluid containing bile the next morning The pain and vomiting had continued from the time of onset The patient had had dysentery 3 years ago, passing blood and mucus in the stools for 6 days In the tropics this is of significance, as amœbic hepatitis is a common cause of acute upper abdominal pain

On examination the upper abdomen manifested a board-like rigidity, more extensive on the right side than on the left The patient's appearance 3 days after the onset of his illness did not support a diagnosis of a perforated gastric or duodenal ulcer The lower abdomen was soft and not tender There was no tenderness over the intercostal spaces, and the liver dullness did not extend above the 5th right intercostal space in the nipple line, making a diagnosis of amœbic abscess of the liver unlikely Temperature 99 8° F, pulse-rate 84, good volume The diagnosis of acute cholecystitis appeared to be correct, and in view of the condition having been present for the past 3 days, subsidence of the inflammation with rest was expected The pain, however, continued throughout the next day, and the clinical picture was unchanged

On the 13th the patient was groaning from severe pain, and a fullness of the right upper abdomen and loin was noticeable The area of tenderness and rigidity had extended down to the umbilicus The lower abdomen was still soft and not tender There was no tenderness in the right loin or over the intercostal spaces There was a well marked area of hyperæsthesia in the quadrilateral defined by Boas below the inferior angle of the right scapula In view of the continued pain and the extension of the area of tenderness and rigidity an operation for acute cholecystitis was advised

The abdomen was opened under light 'Nupercaine' spinal anæsthesia at noon There were filmy adhesions between the stomach and the under surface of the liver with sero pus between the adhesions These adhesions were easily separated The under surface of the liver was normal The gall-bladder was translucent and flaccid The omentum had wrapped itself over the front of the distal half of the stomach On lifting off the omentum, the distal half of the stomach was felt to be indurated, the induration ceasing sharply at the pyloric ring and shading indefinitely towards the cardiac end of the stomach The peritoneum overlying the affected area of the stomach was not much congested The lower abdomen was clean and free from adhesions. The diagnosis of acute phlegmonous gastritis was clear, and, as no surgical measure seemed likely to be of benefit, the abdominal wound was sutured without drainage



Gastric analysis 24 days after operation.

The patient was given an intramuscular injection of sulphapyridine soluble 2 g followed by 1 g of the same drug at 3 PM and 2 g. at 10.30 PM He was also given 1 g of sulphapyridine every 4 hrs up to Feb 17, followed by 0·5 g every 4 hrs up to Feb 21 He made an uninterrupted recovery from the operation, the temperature returning to normal by the 5th postoperative day.

The gastric functions were investigated on March 6 by radiography after a barium swallow The report was as follows. The stomach and duodenal cap are of normal shape The normal mucosal rugæ are shown in the distal half of the stomach. The stomach empties completely in 5 hrs

A test-meal was given on March 9, and the results of the gastric analysis are shown in the accompanying figure An examination of the blood, made on the 11th, showed hæmoglobin, 55%, red cells, 3,470,000, white cells, 7200 (polymorphs 61%, lymphocytes 37%, eosinophils 2%), and slight anisocytosis

COMMENT

Every case of phlegmonous gastritis is of interest. In the case described the preoperative diagnosis of acute cholecystitis appeared to be confirmed by the demonstration of hyperæsthesia in the quadrilateral defined by Boas The recovery of the stomach from the inflammation, as evidenced by the radiographic and chemical tests of its functions, is worthy of record

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LEUKÆMOID BLOOD REACTION

SIMULATING ACUTE ALEUKÆMIC LEUKÆMIA IN A CASE OF PHLEGMONOUS GASTRITIS

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THE term "leukæmoid reaction" was introduced by Krumbhaar in 1926 to cover any condition where the blood-picture closely resembles that of one of the various types of leukæmia Such a blood-picture may be found rarely in many diverse diseases, but particularly in acute infections; the subject is reviewed by Hill and Duncan (1941) and Whitby and Britton (1944) Almost invariably it resembles that of subacute or chronic leukæmia, and it very rarely creates a diagnostic problem The present case simulated an acute aleukæmic myeloblastic leukæmia so closely that the correct diagnosis was not made during life

The patient, a single woman aged 47, a member of the ATS engaged in light work, had always enjoyed good health and was perfectly well until on July 14, 1943, she developed a sore throat, cold, and temperature After five days' treatment with a sulphonamide (identity and dosage unknown) she vomited This illness was followed by weakness, but she had an apyrexial symptomless period of about 10 days She was then admitted to a military hospital with high temperature, headache, and a slight cough, she was drowsy and cerebrated slowly, her mucous membranes were pale and her tongue was heavily coated, the liver was palpable 1½ in below the costal margin, and small soft glands could be felt in the posterior triangle of the neck and in the groin.

Major C Rickword Lane reported on the blood (August 1, 1943) as follows "hæmoglobin 47%, red cells 2,375,000 per c mm, leucocytes 3700 per c mm (polymorphs 5 5%, lymphocytes 35 5%, monocytes 4 5%, metamyelocytes 5 0%, myelocytes 3 0%, myeloblasts or promonocytes 45 0%, smear cells 1 5%) There is a moderate anisocytosis and poikilocytosis One normoblast was seen in counting 200 leucocytes Platelets appear numerous The condition is an acute aleukæmic leucosis"

The patient improved slightly and after five days was transferred to the Middlesex Hospital Her chief complaints were then extreme weakness, cough, and insomnia She was anæmic and pyrexial; glands, liver, and spleen were palpable She became progressively worse, semi-comatose, and eventually irrational During the first few days her temperature was remittent at about 100–102° F, after which it continued at 103–105° F, the pulse and respiratory rates gradually rose to 150 and 50 respectively Her stools were black and terminally she became incontinent of both fæces and urine The blood counts are shown below

The myeloblasts were typical in appearance and approximately 70% showed granules when stained by Washburn's peroxidase method Platelets were 77,000 per c mm

The patient died twelve days after admission, one month after the onset of the illness Autopsy showed no evidence of leukæmia in any organ In the bone-marrow there was a moderate increase in the erythroblastic and myeloid tissue,

but no myeloblastic reaction. The most striking finding was an acute phlegmonous gastritis with ulceration and gangrene; low-grade peritonitis and bronchopneumonia were also present The pathological findings will be published later in detail

We have found only one report (Leibowitz 1938) of a blood picture resembling this one Leibowitz's patient

Date	Hæmoglobin (Haldane)	Red cells (per c.mm.)	Leucocytes (per c.mm.)	Polymorphs	Lymphocytes	Myelocytes	Myeloblasts
Aug 9	51%	—	2000	4%(104)	77%(2002)	2%(52)	17%(442)
Aug 17	33%	1 400 000	1400	8%(112)	40 (560)	2%(28)	50%(700)

had a leucocyte-count between 3200 and 1250 per c.mm. with 40–55% of myeloblasts and premyelocytes The red cells were 2,000,000 per c mm and the hæmoglobin 50%. Radiography of the chest showed the presence of tuberculosis and at the post mortem examination acute tuberculous septic foci were found in most organs

In the present case, the severe and progressive anæmia, the leucopenia, the presence of numerous myeloblasts, the "hiatus leukæmicus" and the clinical findings all pointed to a diagnosis of acute aleukæmic leukæmia As the patient was obviously dying confirmation of the diagnosis by means of sternal puncture was not considered necessary; so the autopsy findings were a complete surprise

Summary—A case is reported of acute phlegmonous gastritis which closely simulated an acute aleukæmic myeloblastic leukæmia

Our thanks are due to Dr G E Beaumont for permission to publish this case to Prof J McIntosh for advice, and to Dr R. W Scarff for the autopsy findings

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POSTOPERATIVE CHEST COMPLICATIONS

CONTROLLED STUDY IN HERNIA AND MENISCECTOMY OPERATIONS

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SINCE Brock's (1936) paper on postoperative atelectasis, many writers, including Campbell and Gordon (1942), Bird, Kilner, and Martin (1943) and Lucas (1944), have drawn attention to the high incidence of this complication after hernia operations, especially in Service personnel The idea is still prevalent, especially among surgeons, that ether anæsthesia increases the incidence and severity of chest complications It therefore seemed worth while to make a critical survey of a carefully controlled series of cases at a Service hospital, using the Oxford vaporiser to standardise the ether anæsthesia, as by this method the percentage of ether vapour used could be accurately recorded

The following series of herniorrhaphies is admittedly only 100 cases, but a small series of carefully controlled cases sometimes has a value lacking in a larger series where all the variables cannot be watched For instance this series was collected at one RAF hospital over two years, then by covering all seasonal changes with the same surgeon (Squadron Leader D F E Nash) the same theatre staff, and all the cases coming from the same ward The operating time was remarkably constant, 30 min any operation taking a longer time or involving any other alteration in technique being eliminated The operation performed in each case was standard McArthur repair All the patients were otherwise quite fit Service personnel, within the age limits of 20–40 years Fifty of the men were anæsthetised with ether and fifty with gas and oxygen

It was necessary to decide on a control operation, and that of meniscectomy was chosen Very often herniorrhaphy and meniscectomy occurred on the same operating list, and it was found that the same time was taken and the same depth of anæsthesia required for either operation. The surgical technique for meniscectomy was easily standardised, and this operation did not involve the abdominal wall As in the hernia cases, these patients were all otherwise fit Service personnel, and the age-groups were the same Here again, fifty patients were anæsthetised with ether and fifty with gas and oxygen

ANÆSTHESIA

A few points in the technique of anæsthesia should be noted, particularly in connexion with the Oxford vaporiser At first, patients anæsthetised with the vaporiser were longer in recovering their cough and other vital reflexes than were those receiving gas-oxygen I soon found it possible to use a much lower concentration of ether vapour than I had thought, and that with the Oxford vaporiser I could maintain a constant light level of ether anæsthesia The commonest mistake made by those first using this apparatus is to run it at too high a concentration of ether vapour, forgetting that the greatest concentration possible in an 'open" method with a mask is 14%

The premedication in all these cases was with 'Hyoscine Compound A' given at least two hours before induction, for which 'Pentothal' 0 5 g was given intravenously followed in the ether cases by ethyl chloride in the induction bag Usually 5–10 c cm of ethyl chloride was necessary before the patient would tolerate 12% ether, at which concentration the apparatus was kept until the incision was made

The average time taken from the intravenous injection to the incision was seven minutes The amount of ether was then dropped to 7–8%, at which level it was kept until the repair was complete or the joint-capsule sewn up It was then switched off completely With this sequence of light premedication at least two hours before operation, a small dose of pentothal and minimal ether all patients had their cough reflexes before leaving the theatre, without resort to such drugs as nikethamide given intravenously

In the gas-and-oxygen cases premedication and induction were the same, the maintenance anæsthetic being nitrous oxide and oxygen in a 'circle closed circuit No suboxygenation was allowed; any case not 'settling" otherwise was given just enough cyclopropane to produce the necessary relaxation

PREOPERATIVE AND POSTOPERATIVE ROUTINE

The patients were all examined by me the day before operation, particular care being taken to investigate any chronic upper respiratory catarrh such as was reported by Morton (1944) to be associated with smoking To the question "Have you any cough?" many patients at first reply "No," but further inquiry often produces the remark "Oh yes, I have the usual smoker's cough in the morning" These patients usually showed no abnormal physical signs in the chest but came to be recognised as particularly liable to postoperative chest complications They were classed as having minor preoperative respiratory complications

In the winter months many men gave a history of recent coryza, and these were not operated on for at least a week after symptoms had subsided Those with a history of chronic bronchitis with sputum or with any chronic respiratory disease such as mild emphysema, were all classed as having major preoperative respiratory complications, even though there were no signs of active disease

An important factor in assessing a patient's condition for operation, though one difficult to define and assess, is his temperament Some patients seem hypersensitive to pain, and these were watched carefully during the first few days after operation to see that they really did carry out the routine, which was as follows

All patients were sat up in bed and made to move about at the earliest possible moment Most patients in this series could do this within two hours of their return to the ward The morning after operation all were seen by a rehabilitation orderly and put through a course of deep breathing and chest exercises Leg movements were also carried out early This was repeated every morning for the whole period of stay in

TABLE II—CHEST COMPLICATIONS AND POSTOPERATIVE VOMITING

Anæsthetic	Herniorrhaphies (100 cases)							Meniscectomies (100 cases)						
	Chest complications				Vomiting			Chest complications				Vomiting		
	Preoperative		Postoperative		Once	More than once	Total no of cases	Preoperative		Postoperative		Once	More than once	Total no of cases
	Minor	Major	Minor	Major				Minor	Major	Minor	Major			
Ether *	21	4	17	8	9	6	15	8	1	8		7	10	17
Gas oxygen *	22	3	18	7	5	2	7	7	1	7		2	5	7

* 50 cases of each anæsthetic

bed, which was 14 days in all cases Temperatures and pulses were recorded four-hourly for the first 7 days The number of times a patient vomited was recorded by observation, not the patient's own statement, as there was often a postoperative amnesia for vomiting

POSTOPERATIVE RESULTS

If a temperature of 101° F was recorded, the patient's chest was at once examined and usually radiographed The only signs ever found were diminished chest movement on one side with an impaired air entry and perhaps an impaired percussion note Radiography usually showed a slight blurring of the costophrenic or cardiophrenic angle, with perhaps patchy areas of loss of lung translucency in the lower lobe The diaphragm often seemed raised.

In no case were the full classical signs of lobar atelectasis found, perhaps because treatment was instituted at once This consisted of a dose of "Mist sod iod ammon" in hot water, followed by deep-breathing exercises to encourage movement of the affected side Incidentally the side of the lung lesion seemed to bear no relation to the side of the operation Usually these measures promptly provoked a fit of coughing, with the expectoration of a small plug of thick viscid sputum, and a rapid improvement in the patient's condition In a few cases it was necessary to give inhalations of oxygen with 5% carbon dioxide before this cough was provoked In the apprehensive type of patient an injection of morphine was a great help The above sequence of events was classed as a major chest complication, even though the temperature only lasted for 48 hours in some cases

The postoperative results are summarised in the tables There were no cases with a temperature over 101° F in the meniscectomies, whereas in the herniorrhaphies there were 15 such cases, 8 having received ether and 7 gas-oxygen The findings are analysed in table II, which shows that there were no major chest complications in the meniscectomies, whereas in the herniorrhaphies the incidence of chest complications was the same whether ether or gas-oxygen was the anæsthetic There was a higher incidence of preoperative chest complications in the hernia series, and the number of cases developing major "chests" was roughly doubled after operation, irrespective of the anæsthetic agent In the meniscectomies the incidence of chest complications was not increased after operation

TABLE I—POSTOPERATIVE TEMPERATURES

Temperature	Herniorrhaphies (100 cases)		Meniscectomies (100 cases)	
	Ether	Gas oxygen	Ether	Gas oxygen
	50 cases of each anæsthetic			
Up to 99° F	14	15	22	22
,, 100° F	21	22	23	28
,, 101° F	7	6	5	
Over 101° F	8	7		

The presence of such a high incidence of preoperative chest complications in cases known to be liable to postoperative chest complications does, however, emphasise the need for a very careful survey of each patient by the anæsthetist before operation, and that reliance must be placed on very careful postoperative routine rather than on the choice of any particular technique of anæsthesia if the incidence of postoperative chest morbidity is to be reduced It is assumed throughout the whole of this paper that the anæsthetist is fully skilled, and that the anæsthesia is thus smooth and uncomplicated in every case

The only postoperative difference, then, which could be attributed to the anæsthetic is a slightly higher incidence of postoperative vomiting after ether (table II) I did, however, get the impression that patients who did not vomit were more liable to develop a "chest," but this series was not large enough to substantiate this. It is a point which is being watched over a large number of cases

CONCLUSION

It is thus evident from this series that the use of ether as an anæsthetic does not increase the incidence of partial collapse of the lung or any other chest complication following hernia operations provided that only the lightest necessary plane of anæsthesia is maintained The Oxford vaporiser provides a ready method of achieving this light level of ether anæsthesia

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CONGENITAL SYPHILIS IN AN INFANT TREATED WITH PENICILLIN

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FEW data are as yet available about the effect and value of penicillin in overt congenital syphilis, and the following case may therefore be of interest

CASE-RECORD

An infant girl, aged 9 weeks, was admitted to hospital on May 31, 1945 On March 15, 1944, her mother had attended the venereal clinic of St Thomas's Hospital with acute gonorrhœa, which responded well to treatment On Nov 13 the mother attended again and reported that her husband, a sailor, was under treatment for syphilis, and that she was 7 months' pregnant *Treponema pallidum* was isolated from a lesion on the labium, and the Wassermann reaction (WR) and Kahn test were strongly positive The mother received 8 injections each of 'Mapharside' 0 04 g and bismuth 0 2 g between that date and Feb 12, 1945 She was delivered of the child in March, her last menstrual period having been in May, 1944 The child weighed 6 lb 2 oz. at birth, and when seen at St Thomas's on April 12 showed no clinical abnormality On May 11, however, both WR and Kahn were strongly positive In spite of numerous postal entreaties the mother did not attend again until May 31 when the child was brought to the Waterloo Hospital because two days previously she had developed a rash, nasal discharge, and dyspnœa

Her weight was now 7 lb 14 oz and the stigmata of congenital syphilis were present The skull had prominent frontal bosses, and was covered with thick black hair, and the upper ends of the tibiæ were tender and enlarged The thorax, buttocks, and body were covered with a scaly polymorphic maculopapular rash, and there was a copious mucopurulent bloodstained nasal discharge The respiratory-rate was 36, and moist sounds were heard in all areas of the chest The liver was not felt

The temperature rose rapidly to 106 5° F, and the respiratory-rate to 70 An area of impaired resonance with tubular

breathing appeared on the day after admission at the right base, extending up the spine The child was at first placed in an oxygen tent, but with the onset of hyperpyrexia this was discontinued, and oxygen could not be given through the obstructed nose.

Sulphapyridine 1 75 g had been given in divided doses during the first 12 hours, but on the second day this was changed to penicillin sodium 38,000 units 4 hourly by intramuscular injection, with brandy 5 minims 4 hourly Gradual improvement in the general condition took place, and after 412,000 units had been given the penicillin was discontinued. The temperature thereupon rose to 107° F, falling soon after to 102° F, the general condition remaining unchanged.

The blood-count on the second day of admission had shown 12,900 white cells per c.mm. (finely granular polymorphs 28%, eosinophils 2%, coarsely granular polymorphs 2%, lymphocytes 50·5%, hyalines 14 5%, transitionals 1%, myelocytes 1 5%, and myeloblasts 0·5%) The red cells numbered 3 200,000 per c.mm. and were very irregular in shape, with many basophils and normoblasts.

Penicillin 9500 units 4 hourly was started again on the 6th day In 24 hours the temperature had fallen to normal, the nasal discharge had ceased, and the pulmonary signs had begun to clear A further 95 000 units was given before stopping the drug, on the 8th day The temperature however, again rose, and there was a slight return of the nasal discharge The epiphyses were larger and very tender Potassium iodide gr 3 was given t.d and as the temperature continued to swing in spite of the improvement in the general condition, 'Acetylarsan' 0·5 c.cm on every 3rd day with pulv hydrarg o creta gr ¼ t.d and inunction of ung. hydrarg nit fort to the abdominal wall was begun In all four injections of acetylarsan were given The respiratory rate was still high, but pulmonary signs were almost absent The temperature range was lower (100 -102° F)

On the 21st day penicillin 9500 units 4 hourly was recommenced Once more the fall in temperature to normal was immediate, and after a further 95 000 units it remained down.

The WR at the end of the first course of penicillin was strongly positive After two further courses it remained positive, but the specimen was too small for a quantitative test

On June 28 a further course of 100,000 units spread over 3 days was begun At the end of this course all medication was stopped and on July 7 the WR was completely negative with a negative Kahn The child continued to thrive and gain weight. Its epiphysitis subsided, and its cry became normal It took a normal interest in its surroundings but there was a convergent squint and visual response to light was poor Ocular movements, however, were full, and fundal changes were not seen

Between the time of admission and the change in WR 702,000 units of penicillin had been given, together with acetylarsan 2 c.cm mercury and potassium iodide

Since her discharge in July the child has been readmitted once with an attack of bronchitis accompanied by diarrhœa Recovery was rapid and a repeat WR remained negative The convergent squint persists, but vision appears to be present, and there is no choroiditis. Apart from the setback of this second short illness, progress is good.

DISCUSSION

It was difficult to say how far the result in this case was due to the penicillin administered, since ancillary treatment was given. It was felt that the child's condition did not admit of experiment.

The most striking effect of the penicillin was in the control of the initial bronchopneumonia and of the florid syphilitic symptoms, such as rash and nasal discharge, which invariably subsided during the courses tending to recur afterwards in a decreasingly severe form During the later courses, when pyrexia was subsiding, each administration of penicillin was followed by a striking fall in the respiratory rate and a disappearance of lethargy; but, like the remissions in the secondary symptoms, these continued only so long as the penicillin was given

It is noteworthy that no less than 600,000 units was given without significant quantitative change in the Kahn test Another case of established congenital syphilis in a child of 9 years, treated at this hospital showed no diminution in Kahn reaction four weeks after the administration of 500,000 units intramuscularly in 5 daily doses The 'burst' method of administration was selected originally in view of the difficulty of obtaining continuous supplies, and it seems likely that a far more rapid cure would have resulted from a more continuous administration

No regression in the bony lesions could be noted radiographically with successive courses, but clinically there was freer movement and less tenderness after the later courses, and this improvement was maintained

Since acetylarsan and mercury are well tolerated by infants, there seems to be little doubt that in acute cases the combined therapy remains at present the method of choice It is interesting to compare the readiness of the response shown by the bronchopneumonia in this case with the relative resistance of simple infantile bronchopneumonias treated with penicillin Although there was no conclusive evidence that the chest condition was a syphilitic process, the clinical signs bore little resemblance to those of an infantile bronchopneumonia due to cocci The respiratory sounds were drier and more like the crepitations of an early apical tubercle, and all the signs more migratory from day to day No residual shadows or fibrosis could be seen at the time of writing

SUMMARY

A case of exceptionally severe infantile syphilis was treated with short courses of penicillin in association with the usual antispecific drugs, with good result

I wish to thank Dr Bernard Myers for his permission to publish this case the treatment of which he supervised throughout, Dr T Anwyl Davies, of St Thomas's Hospital, for the data relating to maternal treatment; and Sister Wilmshurst for her expert nursing and accurate records.

Reviews of Books

The Background of Penicillin

Microbial Antagonisms and Antibiotic Substances, SELMAN A. WAKSMAN, professor of microbiology, Rutgers University, microbiologist, New Jersey Agricultural Experiment Station (Commonwealth Fund Pp 350 21s 6d)

Professor Waksman's valuable and timely book shows that the antibacterial action of penicillin is only a particular example of an extremely common state of things. Pure cultures of micro-organisms in the laboratory are artefacts, under natural conditions all kinds of life—bacteria, fungi, protozoa, plants, and animals—are jostled together, and promote or hinder each other's survival. Nowhere is the jostling of organisms so vigorous as in the soil and it is to the inhabitants of the soil and their biological interrelations that the first parts of the book are devoted The many different ways in which organisms living together can influence each other's growth are briefly indicated and antagonism by the production of the so-called "antibiotic" substances is considered in detail The word "antibiotic" is not a happy neologism, but it is already so well consecrated by usage that it is unlikely to be replaced He describes the bacteriological methods of detecting organisms which produce these substances of isolating the organisms and their products, and of measuring the extent of the antibiotic effect Antibiotic substances have been prepared from many different orders of life—bacteria actinomycetes, fungi, and even animals and plants—but to date the most important sources have been found among the fungi (especially penicillium and aspergillus) and among the actinomycetes So far 34 antibiotic substances have been identified and studied but undoubtedly these are only the beginning of a much longer series Chemically, those identified have been found to be very varied They include lipoid like bodies (pyocyanase) pigments (pyocyanin), polypeptides (gramicidin), sulphur bearing compounds, quinones, and organic bases (streptomycin). Their modes of action are also very varied, though knowledge here is rudimentary, and there is great scope for fundamental investigation. Disease control by antibiotics has been mainly limited so far, to the use of penicillin which has achieved such brilliant success as to outweigh all other disappointments.

The value of the book lies in its broad survey of the whole field Against this background the specialist on a particular problem can build up his own collection of research data Each biological aspect is discussed as it

concerns individual antibiotic substances, and though this arrangement makes it difficult to collate all the information given about any particular substance it avoids repetition The work of earlier years is better reviewed than that of the past two years, which may disappoint readers seeking up-to-date information The conspicuous reticence about the chemical nature of penicillin is presumably due to war-time secrecy rules under which this knowledge has been acquired Other omissions may be due to inevitable delays between compilation and publication, but the silence about streptomycin is curious This substance is therapeutically the most hopeful antibiotic after penicillin, and it has been isolated and studied by Professor Waksman himself; yet information about it is scanty throughout the book

Rebuilding Family Life in the Post-War World

An enquiry with recommendations. Editor SIR JAMES MARCHANT (Odhams 2s)

THIS is a book of ten chapters by nine authors, most of whom sheer off from the subject into essays on population statistics, or economics or genetics, or nutritional policy, or the education system, or the structure of the health services It is left to Dr Margaret Hadley Jackson, Dr Eliot Slater, and the Right Rev. Dr Hagan to get down to it, and of these the Moderator of the Church of Scotland rings truest He speaks of the revolt against the restraints, sacrifices, and duties of family life, and lays this mainly at the door of the excessive individualism which has marked the thought and practice of the last half century Dr Hagan's diagnosis is that we no longer recognise that the foundations of marriage and the family are ultimately spiritual, laid in a right understanding of man, his nature, and his life His recommendation is that the State should remember in all its legislation and administration that the unit of human existence is not the isolated individual but the family.

Other contributions in this book present economic plans for family allowances and readjustment of taxation, and ask for home helps, free school meals, better housing, more maternity and child-welfare work, the raising of the school age, and abolition of privilege in schools They hope for a wider study of social medicine, for the training of boys and girls in parenthood—with emphasis on the interest of rearing a family—for discussion groups, for instruction in the use and abuse of contraceptives and on the dangers of criminal abortions, and for the establishment of marriage-guidance centres

March of Medicine

New York Academy of Medicine Lectures to the Laity No IX (Oxford University Press Pp 121. 11s 6d)

THESE six lectures, rich in content of fact and figure, and covering a great deal of ground, are written in a style which makes them easy and pleasant reading Prof C. M McLeod gives a penetrating and lucid exposition of the development of chemotherapy from the time of Ehrlich to the present day Lieut.-Colonel T. T Mackie traces from classical times the influence of epidemic disease on military and naval expeditions and on the rise and fall of nations Sir Gerald Campbell, our Minister in Washington, in an essay on the effects of science on man, brings a vigorous style to the expression of much shrewd philosophy, his theme being that while science has freed, enriched, prolonged, and accelerated human life it has also complicated it dangerously. "We have still to conquer the lawless forces of human nature if we are to harness science constructively for the building of that new order of which everyone dreams"

New Inventions

SUSPENSION BAR FOR THOMAS SPLINT

A SUSPENSION bar (PVMS India no. 08326), which can be applied in a matter of seconds, and which firmly fixes the Thomas splint without tying, is illustrated in the accompanying figures

The Thomas splint is applied in the usual manner, and the patient placed on the stretcher When the splint is on the right leg, bearers 1 and 2 kneel on their left knees at each end of the stretcher, and press their right feet against the side of the stretcher Bearer 1 turns the bar flat with his right hand Bearers 1 and 2 then lift the end of the Thomas splint, and bearer 1 slides the suspension bar on to the splint so that the outer side of the splint passes to the outer side of the hook between the bracket and the frame Bearer 1 rotates the bar, pinching the splint between the bracket and the frame It is fairly easy to clip the bar on to the stretcher if the bar is strongly rotated so that the flattened base is brought parallel to the stretcher surface (fig 2) This is done as follows Bearer 1 rests his right hand on the end of the Thomas splint, and grips the splint side of the bar with his left hand. Bearer 2 holds the suspension bar bracket on his own side with his left hand, and the flat base with his right Both bearers rotate the bar, bringing the flat base horizontal,

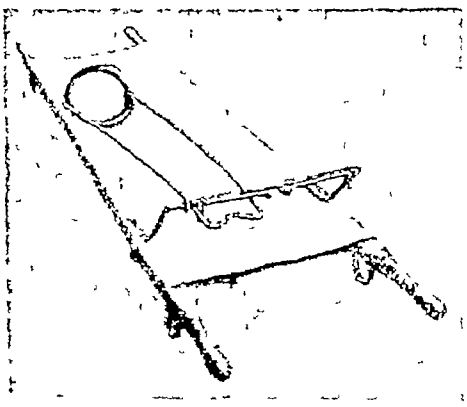
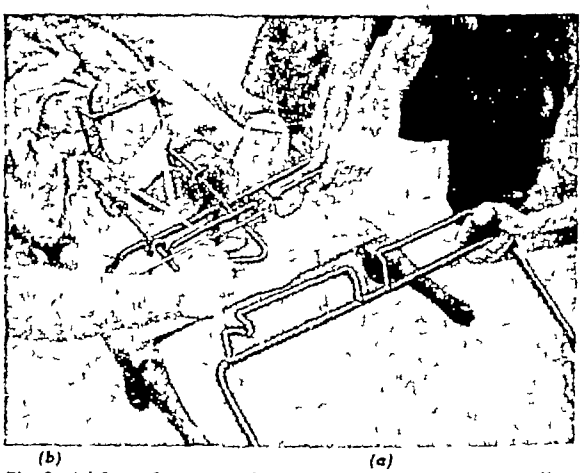


Fig 1—Suspension bar applied to a Thomas splint.



(b) (a)

Fig 2—(a) Stage 2: Suspension bar ready to be slid on to splint. (b) Stage 6: Suspension bar has been slid on to the splint, and rotated to bring the flattened base parallel to the stretcher The splint side-clip of the suspension bar has been applied The opposite clip is in the process of being applied

and the splint side-clip is pushed on to the stretcher side The other clip is then pulled out to just beyond the side of the stretcher, released, and if necessary tapped into position with the hand. The splint is now firmly locked

In order to remove the bar, the movements described are reversed, the side opposite the splint being removed first Since soft iron is used for this device the bar opens a few degrees when it is removed, and this distortion is rectified by bending the bar frame back by hand to its correct angles

The bar is sloped to allow greater freedom for the bearers' hands when a tall patient is carried

When the Thomas splint is resting in the suspension bar without bearing weight, it lies just above the horizontal plane When it bears weight, the ring is depressed and the slight bending of the splint causes it to be firmly pinched, which prevents movement in the line of the splint

M S HOLMAN, M B LOND
Lieut -Colonel RAMC

THE LANCET

LONDON SATURDAY, OCTOBER 6, 1945

The Royal Commission on Population

THE debate on the birth rate began about twelve years ago It was not too soon, for the rate of human reproduction in Britain had already been declining for over fifty years It had fallen by 60% It was leaving us poorer by some 100,000 children every year

To the Governments of the 1920's and the 1930's the immediate results of this trend were helpful They assisted in keeping infant and maternal mortality to a respectable figure, they made it unnecessary to hurry forward with plans for new maternity homes to match the rising demand for institutional confinements, and they meant that the problem of classes of 40 and more children in State schools would, in the end, solve itself Indeed no Government embarking on a population policy can hope to benefit financially during its lifetime, on the contrary, any Government public-spirited enough to enact long distance legislation concerning the family is going to be unpopular with the general taxpayer Fathers and mothers may be enthusiastic but they will soon be outnumbered by people who have long since passed the reproductive period

When the Coalition Government appointed a Royal Commission in March, 1944, the terms of reference were drawn widely enough to cover all these subjects The Commission were asked "to examine the facts relating to the present population trends in Great Britain, to investigate the causes of these trends and to consider their probable consequences, to consider what measures, if any, should be taken in the national interest to influence the future trend of population, and to make recommendations" Now, eighteen months after their appointment, they have issued a clear and forthright statement[1] about their work, their future activities, and the conclusions already reached In a brief and lucid account of the mechanism of population change they show no uncertainty Discussing the trend up to the outbreak of war, they say that "it appeared extremely probable that the population of Great Britain would shortly begin to decline" This is very different language from that of a white paper[2] published by the same Government in 1942 when the birth rate was 20% lower than today Then the tone was brightly optimistic, the unofficial experts (if we may call them that) were frowned on, and it was suggested that a decline in population was not likely to begin for at least twenty years Evidently the Royal Commission do not share this opinion of 1942 They hold that if the future volume of births continues to decline, "the effect on British social and economic life, on migration to the Dominions, and on Britain's position among the nations, will be far reaching And behind all these considerations lies the ultimate threat of a gradual fading out of the British people This threat, though remote at present, is real, and it overshadows the whole problem"

After a review of long-term trends, the report examines the striking rise in the birth rate since 1941 The number of births registered in Great Britain in 1939 was 706,000 The figure dropped to 693,000 in 1940 and to 669,000 in 1941 Then the tide turned, and the number rose to 745,000 in 1942, 778,000 in 1943, and to 841,000 in 1944 This movement is in sharp contrast to the experience during 1914–18, and no complete explanation is offered It is suggested, however, that the abnormally high level of marriages during the past decade has played an important part, and it is pointed out that the birth rate has risen, not only in Britain but in many European countries, as well as in the Dominions and the United States (the figures were given in these columns last July)[3]

The purpose of this review of population trends is to introduce the chief point of the report—namely, that many more facts are needed We are indeed appallingly ignorant about such matters as the incidence of childlessness, the distribution of families of various sizes, the spacing of births, and fertility differences between occupational and social groups A few of the exports have been saying this kind of thing for years They have told us that the first (and only) fertility inquiry was made as long ago as 1911, and that a great many vital statistics that have been collected have not been published. It is excellent news that some of these deficiencies are now to be remedied An investigation has, for example, been started by the Biological and Medical Committee of the Commission (assisted by the Medical Research Council and the Royal College of Obstetricians and Gynaecologists) into certain aspects of sterility What apparently is also wanted, to obtain additional fertility data, is a complete family census But this, in the Commission's opinion, is not practicable at the moment We are not told why The last census was held in 1931, it was impossible to hold one in 1941, and if we have to wait another six years the results will not be available until about 1954 Yet April, 1946—midway between 1941 and 1951—seems to be the appropriate time We cannot wait until conditions return to normal—whatever that may mean If the Government of India can carry out a census of 350 million people and publish the results in 49 volumes within 2½ years, it should not be any harder to overcome the difficulties of census taking in Britain in 1946

However, the Commission are proposing in place of a family census to obtain the information they need from "a representative sample of married women," and they intend to ask for the coöperation of wives and mothers in a voluntary family census Until the additional data on fertility are available it seems that they cannot make much headway with their work It is to be hoped therefore that the help they need will be readily forthcoming, and that the results will be published so that the general public can take part in debating this momentous question

1 Statement by the Royal Commission on Population HM Stationery Office September 1945
2 Current Trend of Population in Great Britain, Cmd. 6358 May, 1942

3 *Lancet* 1945 ii 11

The Injured Back

STRAINED backs are common, and in organised communities of industrial workers and Servicemen their ineffective treatment results in a serious loss of man-hours What is the pathology of an acute low back strain? Is it a simple myofascial injury, or a deeper lumbar and lumbosacral strain, and if the latter, are we to regard intervertebral disk prolapse as an integral part? It would be stupid to refuse to admit that there may be several different local lesions, but equally short-sighted to ignore the increasing recognition of lumbosacral strain with associated disk prolapse as a causative factor

MARBLE and BISHOP[1] observe from experience with a large American insurance company dealing with workmen's compensation that industrial back injury is common and the results of treatment vital to the future of the workman The costs of compensation and of medical care are a fair index of the success of this treatment Of their 500 cases of suspected disk prolapse, 92 were verified by operation, all with a history of indirect trauma A third of the patients operated on returned to their former work within 6 months, and a tenth within a year In the remainder results were poor, the great majority of failures occurring in those submitted to spinal fusion as well as removal of the disk Final assessment showed costs to be directly proportional to the type of result, the total medical and compensation expenses of a poor result being six times those of an excellent case ADSON'S[2] operative results are better than these, with 88% experiencing complete relief, as is usual, his compensation cases were slowest in recovery, with nearly three times the failure-rate The good results described by BURNS and YOUNG in this issue speak for themselves An obvious comment[3] on these findings is that there have been prolapsed disks for thousands of years, that we have lived with them unbeknownst until 5 or 10 years ago, and that we are still ignorant of the 10-year end-results And the good results of treatment obtained in the 5-year period of prosperous full employment just ending may be misleading, there may well be more compensation and disability in a time of scarcity[4]

The relation between back strain and disk prolapse must be put into proper perspective. It is often impossible at the outset to tell whether a strained back will be trivial or protracted and incapacitating MURRAY[5] found in an ordinary factory medical service that despite its frequency the total time lost annually over back strain was only some 2 weeks per 1000 employees, and only 8% of DOUGHERTY'S cases[6] did not return to work within 5 days—figures which seem surprisingly low until we recall how a trivial injury often crops up in the history of a patient with severe disk prolapse The factory physician or the unit medical officer is mainly concerned with palliation and return to duty, and most of his cases are undoubtedly minor. Any subsequent disability or sciatica is either not related by him to the previous injury or is first seen by an outside specialist The industrio-legal aspect is not clearly defined As CYRIAX points out in this issue, changing views on the pathology increasingly throw the onus on disk prolapse as the cause of lumbago, and will tend to place the responsibility on the employer. In many cases where low back pain and sciatica develop within a reasonable time after even a trivial, but specific, working injury, they may be clearly attributable, and this is not invalidated by the knowledge that trauma may be only the last step in a long degenerative process Certainly, compensation settlement is on a sounder basis after operative proof, for though the ordinary litigant is as yet unfamiliar with the symptoms of disk prolapse, he is unlikely to remain so

As far as treatment is concerned, too much time is still wasted in physiotherapy of a useless or even a provocative kind From any angle, whether of State, employer, or employee, it is important to extract from the many cases of acute back strain those which may well have prolapsed disks, and keep them from developing further Plaster immobilisation, as described by CRISP in these pages, is probably the best method, it permits intensive re-education of the long spinal muscles and often an early return to work Acute cases treated on these lines have a fair chance of cure, but need protection for at least 3 months However small a proportion disk prolapse may form of industrial back injury, it is of value to the community to adopt this prophylactic viewpoint, the 4% of proved cases quoted in GORDIN'S series[7] is not a small figure in terms of time and money wasted in delay

It is the unrecognised cases and the failures that may need subsequent operation While it is probable that too many cases of low back pain and sciatica are operated on in the United States when other conditions are responsible, it is also probable that the more conservative of British surgeons are too conservative, delaying until all palliative measures have failed, and in some cases disbelieving in the lesion itself This ultraconservative attitude does a lot of harm And it arises partly from unwillingness to learn the technique of a newish operation—one moreover which should be regarded less as a major intrusion into the fundamental recesses of the body than as a routine procedure like the removal of a semilunar cartilage Indeed, these are closely comparable lesions, and success in both depends on early diagnosis and operation before the joint has suffered its internal derangement too long, and on the re-education thereafter of the guarding spinal or quadriceps muscles, as LEVAY[8] has pointed out The operation itself has no mortality in the ordinary sense of the word, and can hardly be said to present the great technical difficulties ascribed to it by CYRIAX All that is necessary is to remove the ligamentum flavum at the lumbosacral interspace on the affected side, with just enough, if any, of the adjacent bone for clear access; and if the prolapse is not found at this level to repeat the process at the space above—a procedure which locates 95% of all lesions There is no need for the formal laminectomy or hemi-laminectomy advocated by some authorities[9]—the operation can often be

1 Marble, H C, Bishop, W. A *J indust Hyg* 1945, 27 103
2 Adson, A W., in Lectures on Peace and War Orthopedic Surgery, Michigan, 1943.
3 Oldberg, E *J indust Hyg* 1945, 27, 105
4. Magnuson, P B *Ibid*, p 108
5 Murray, H G *Indust med* 1943, 12, 730
6 Dougherty, W *Ibid*, 1942, 11, 473
7 Gordin, A. E *Ibid*, 1942, 11, 18
8 LeVay, A D *Lancet*, 1944, i, 116
9. Watson-Jones, R Fractures and Joint Injuries, Edinburgh 1943, p 370

done without removing any bone at all—and excellent results are obtained by a willingness to perform what is virtually an exploratory operation, as is eloquently demonstrated by BURNS and YOUNG On the question of fusion it is impossible at present to be dogmatic, certainly it is rarely indicated for the working man or serving soldier under present conditions What is needed is to cut out the extra physical and emotional stresses of long immobilisation by a revolutionary method of securing rapid stable fusion, and this we have not yet got, although such devices as the liberal use of cancellous bone,[10] screwing together the lumbosacral facets,[11] or the clothes peg graft[12] may be useful

There are strong economic indications for operation in the wage earner, like those long recognised to apply to surgical intervention in chronic peptic ulceration For the importance of the subjective factor cannot be overrated, hence the evils of procrastination as a potent cause of neurosis It is true that many neurotics complain of backache but very often an unrelieved low back pain or sciatica will precipitate neurosis in the sufferer, and it is within our power to prevent this altogether in many cases But the whole interrelation of neurosis and back trouble is one of those psychosomatic entities which cannot properly be artificially dissected The vertebral neurosis has been well described by FETTERMANN,[13] and we must understand it not merely in terms of the gross hysterical spine, with which CHARCOT made our fathers familiar Psychoneurotic myasthenia and fatigue may be superimposed on physical discomfort so as to secure escape from an intolerable work situation These neuroses occur much oftener in industrial cases than in ordinary practice A labourer whose back muscles are sore from hard work, with an unhappy home life, or troubled by insecurity and fear of poverty, may accumulate resentment against society or employer, and will tend to utilise an injury to his back as a nucleus for the crystallisation of these forces and to gain attention and sympathy As an escape from an unhappy work situation this is at least as effective as a gastric neurosis, the other major partner in the subjective illnesses of those industrial and military organisations in which some degree of chronic frustration must prevail "I can't carry on, my load is too back breaking" is precisely equivalent in its symbolism to the I can't stomach this situation of the dyspeptic[14]

Orthopædic surgeons like other clinicians, are learning that a purely physical approach to these cases leads nowhere They need a psychiatric social worker at the other side of their outpatient table who will take up the work where they leave off It is not a question whether a patient has an "organic" lesion or not, but of estimating the relative proportions of the physical and psychological factors in each case Does the patient need surgery only, or personal adjustment, or both, and how much? We require, when demobilisation allows, a social service attached to all our hospital departments on the lines already developed in the States, where the whole family circumstances of patients can be reviewed, and to some extent adjusted[15] All this is inseparable from the changes in social insurance and the increasing communal responsibility for sickness and unemployment that are only at the early stages of their evolution

Miners' Pneumoconiosis

MINES and the miners are of special interest at present The householder is anxious to know whether he will get enough coal to keep warm this winter, the social economist is concerned with the methods and results of the proposed nationalisation of the mines, the industrial psychologist must estimate the effect that nationalisation, first in prospect and then in action, will have on output But underlying all these questions is the miner himself his personal risks to limb and lung, and how these can be mitigated

In 1936, at the request of the Home Office and Mines Department, the Medical Research Council began a series of investigations (under the direction of their committee on industrial pulmonary disease) into the problem of chronic pulmonary disease among coalminers, with particular reference to the South Wales coalfield Two reports of these investigations have already appeared The first,[16] in 1942, described the clinical, radiological, and morbid anatomical features of the pneumoconiosis of coalminers as seen in South Wales The second,[17] in 1943, rightly accepting the findings of the first that air borne dust must be primarily responsible for the lung condition, provided a detailed account of the chemical and physical characters of the dusts which the miner breathes and of the coal seams and adjacent rocks which he hews A third,[18] just published describes experimental studies, and, like all good experimental work, though it answers some questions it asks others, remarking that "despite the great amount of information elicited, many doubts and discrepancies have still to be dispelled, and the committee feel that it would be imprudent at this juncture to draw any conclusions"

Three main lines of research have been followed Prof E J KING and Dr NAGELSCHMIDT describe the nature of the mineral content of the lungs of 54 South Wales miners, 40 of whom had been studied histologically in the first report They found that the proportions of coal and siliceous material were almost identical with that of the air borne dust at the coal face, and these proportions reflected the particular branch of the industry and dust exposure of the worker Next an attempt was made to correlate the type of histological lesion with mineral content BELT and FERRIS grouped the pulmonary lesions into four types—dust reticulation confluent fibrosis mixed nodulation and silicotic nodulation KING and NAGELSCHMIDT have found no relationship between lung histology and the concentration of coal or kaolin The concentration of mica and quartz, on the other hand, ran parallel with increasing fibrosis but there was not necessarily a higher content in the two intermediate groups of morphological lesions than in reticulation, which is regarded as the mildest type of lesion On the whole they are against the view that "clean"

10 Mowlem R *Proc R Soc Med* 1945 38 171
11 King D *Amer J Surg* 1941 56 257
12 Bosworth D M *Surg Gynec Obstet* 1944 78 19
13 Fettermann J L *Psychosom Med* 1940 2 265
14 Alvarez W C *J Amer med Ass* 1938 92 123
15 Richardson H B Patients have Families New York The Commonwealth Fund 1945
16 *Spec Rep Ser med Res Coun Lond* No 243 *See Lancet* 1942 1 689
17 *Ibid* No 244 *See Lancet* 1943 ii 205
18 *Ibid* No 246 HM Stationery Office 1945

coal can produce a tissue change in the lung, but "clean" coal is an artificial product of the laboratory and "pure" coal such as a high-quality domestic fuel, contains quite a proportion of siliceous matter, and the lungs of trimmers—the men who load coal into ships and are exposed to very little rock dust—contained abnormal quantities of silica though there was no more coal there than in the colliers KING and NAGELSCHMIDT do not feel that kaolin plays any positive part in the production of lesions, but as to whether both quartz and mica (sericite) are involved it is more difficult to say The concentration of both increases with the severity of the lesions, and there is good evidence, both from other forms of pneumoconiosis occurring with sericite-free dusts and from animal experiments, that quartz is a fibrosis-producing agent The rejection of mica is not based on the statistical correlation between analysis and histology but on the apparent inertness of South Wales mica when injected into animals Another question of great importance which is raised is why lungs containing large quantities of quartz show only reticulation without any formation of silicotic nodules. Of this two possible explanations are put forward either the quartz is so diluted with other inert dusts that its characteristic effects are not produced, or the other dusts are not inert, but lower the solubility of the quartz by coating it with a layer of alumina and so reduce its noxious effect—a view supported by evidence from other experiments recorded in the report

The second investigation, by the late Dr BELT and Professor KING, is a continuation of the work of the late Prof E H KETTLE, FRS, in which various dusts were injected into the lungs of animals and their effects compared The various lesions in the animals' lungs are clearly described The initial reaction, irrespective of the nature of the dust, is phagocytosis, and, if the dust is inert, some degree of foreign-body reaction develops, with a minimal increase of reticulin fibrils but no collagen If the dust is not inert there is an inflammatory reaction characterised by fibrinous exudate rather than an outpouring of neutrophils This is followed by a process of organisation which is reminiscent of the carnification of an unresolved pneumonia, and includes a great increase in reticulin fibrils without actual collagen fibrosis such as is seen in man These observations on the initial lesions, when uncomplicated by infection, naturally raise the question of what is the proximate reason for the tissue change Mechanical irritation by the dust particles has long been rejected it is now generally felt that silicic acid is formed as the result of the solution of the noxious dust, and that this is "irritative," but in reality this only takes the mechanical irritation hypothesis a stage further, and it seems desirable to determine whether the silicic acid increases capillary permeability and so allows the exudation of fibrin, or whether it acts on ground substance and so alters its physicochemical characters that collagen sol is converted into fibrillary reticulin Such a study could be pursued in vitro, and would be analogous to the observations of HERINGA that precipitation of reticulin fibrils from a weakly acidified solution of collagen is conditioned by the addition of different salts resulting in a coarse or a fine reticulin network In the experiments now reported it was found that "pure" coal produced a foreign-body type of reaction with a minimal fibrosis, with some emphysema simulating the chest reticulation of coal miners Coal dusts mixed with siliceous material usually produced some degree of organisation and reticulin proliferation, the dusts containing mica and kaolin with even small amounts of quartz produced considerable change, whereas those that contained shales appeared to inhibit the action of the quartz, so that the degree of fibrosis was less with the same proportion of pure quartz With stone dust there were similar findings, shale dusts giving a minimal reaction and quartz dusts a pronounced one An isolated fraction of sericite produced a minimal reaction, but this dust had been treated rather drastically to make the particles of uniform size, and sericite from a source other than South Wales produced a sharp reaction, so indeed did a kaolin, but this was found not to be pure, since it contained a high proportion of silica When artificial mixtures of dusts were used it was again found that shale or coal reduced the reaction which would have occurred with the quartz alone

The third group of experiments carried out by Professor KING deal with the solubility of dust from the mines It was found that all these dusts had low silica solubilities, releasing much less silicic acid than their quartz content would lead one to expect. Mixtures of shale and other dusts reduced the solubility of quartz, and this was apparently the result of deposition of a protective coating of aluminous substances on the surface of the particles "Clean" coal reduced the solubility of quartz, but this was due to the minerals contained therein and not to the coal substance itself A curious and apparently anomalous finding, in view of the fact that pneumoconiosis is much more severe in anthracite than other coalmines, was that anthracite reduced the solubility of quartz more than other coals did, on the other hand, where the mineral content of the anthracite and other coals was separated, they were equally active. KING puts forward the ingenious hypothesis that in some way bituminous and steam coal inhibits the solubility of the siliceous matter contained therein, whereas anthracite has not this property of combination, and so its mineral content can produce its effect either (under experimental conditions) by inhibiting the solution of added quartz, or (under natural conditions) by not preventing the solution of siliceous material as other coals do

KETTLE always pointed out the fallibility of the test-tube or animal experiment when directly applied to man, and his successors are well aware of this The complicating factor, to the experimentalist, of bacterial infection has purposely been excluded from these experiments, but exposure to respiratory infections—not only tuberculosis but the ordinary coughs and colds to which the miner, like everyone else, is exposed—cannot be excluded where the natural disease is concerned However, the presentation of the results of these "clean" experiments should not be ignored because they are unnatural, they form a solid foundation on which further work can be built, by observations in both man and animal, and we shall look forward in a few years to the first reports from the new MRC research unit which has been established at Cardiff under the direction of Dr

CHARLES FLETCHER What the present experiments do show is that, even excluding infection, the interaction between the dusts and the lung is extremely complex, and that the noxiousness of a dust does not solely depend on its silica or quartz content, but is influenced for better or worse by the other components of the dust

Annotations

NUFFIELD HELP FOR DENTISTRY

THE Nuffield Foundation have lately shown a generous interest in the advancement of child health and industrial health They are now offering the same practical help to teaching and research in dentistry Grants for research totalling £9000 a year for ten years are being made to the dental schools of the universities of Durham Leeds, and Manchester, and of Guy's Hospital Nuffield dental fellowships have also been created which will be open to qualified dentists, and to graduates in medicine and science who wish to train as teachers or research workers The annual value of a fellowship will be £400–800, and it may be awarded for one or more years, but as a rule for not longer than three years Travelling expenses will be paid to fellows who go abroad for study A few scholarships will be available for dental students who, in the opinion of their school would profit by receiving, during their training, additional instruction in anatomy and physiology A scholarship will normally be tenable for only one year, but may be renewed for a second year It will provide tuition fees and a subsistence allowance not exceeding £200 a year Forms of application may be obtained from the secretary of the Foundation 12–13, Mecklenburgh Square London, WC1

USE OF SULPHONAMIDES

IN 1943 the Medical Research Council first issued its *Medical Use of Sulphonamides*; and since then more than 50,000 copies have been sold We hope that the second edition[1] edited by Dr F Hawking and Dr F H K Green, will have an even larger sale; for nobody who employs sulphonamide drugs can afford to be without this excellent summary of current knowledge If today these potent remedies are still abused it is not for want of good guidance

In the new edition this guidance is of course given from greater knowledge of sulphonamides and their action But the memorandum has also been brought up to date in two other respects. It takes account, first of the increasingly widespread use of penicillin, and secondly of the introduction of various new sulphonamides and related drugs To avoid overweighting, details of only three new preparations have been given—namely, phthalyl sulphathiazole, 'Sulphamerazine,' and the German 'Marfanil' The two last it will be seen appear under the names bestowed by their makers, for they have not yet received official names in this country; but this is without prejudice to the principle that 'where official or common' names are available sulphonamides should not be ordered or prescribed by proprietary or brand names the use of trade names to describe these drugs is liable to make both for confusion and for difficulties of supply' This is a rule that we have repeatedly commended to our readers, and indeed to manufacturers[2]

The activity of a sulphonamide is related to the amount of ionic dissociation it undergoes at the reaction of the body fluids For example sulphathiazole, which is about 50% dissociated is thus some 3000 times more active than sulphanilamide

"Although for this and other reasons the action of some sulphonamides is *quantitatively* greater than that of others, there is little evidence for a *qualitative* difference apart from the exceptional case of 'Marfanil,' which has an entirely different mode of action In the opinion of most workers, the fact that sulphanilamide is effective against streptococci, sulphapyridine against streptococci and pneumococci, and sulphathiazole and sulphadiazine against streptococci pneumococci and staphylococci is due not to the action of any particular drug being specific for certain organisms, but rather to the less susceptible organisms such as pneumococci and staphylococci, responding only to the more active compounds

"On the other hand the differing rates of absorption and excretion do render the use of certain compounds advantageous for certain types of case, thus, sulphanilamide, on account of its ready solubility, is useful for local application to wounds though the less soluble sulphathiazole has greater bacteriostatic power sulphadiazine produces particularly high blood concentration because of its slow excretion while sulphaguanidine is effective against organisms in the lumen of the lower part of the alimentary canal because it reaches this region in high concentration, owing to its slow absorption.'

It follows that once organisms have become resistant to one sulphonamide compound they are resistant to all the others with typical action (marfanil is an exception) But the more active drugs such as sulphathiazole may still show some antibacterial action when the less active, such as sulphanilamide and sulphapyridine, have failed

On absorption into the blood stream sulphanilamide is distributed pretty equally through the body Sulphapyridine, on the other hand, accumulates in the liver and the distribution between plasma and corpuscles and between plasma and cerebrospinal fluid, varies with the different drugs Thus if the concentration in the plasma is 1 0 the concentration in the CSF is sulphanilamide 1 0, sulphapyridine 0 7, sulphathiazole 0·15–0·4 and sulphadiazine 0 5–0·8. (These differences may be due to part of the drug being bound to the plasma proteins) Setting out clearly the tactical use of the various compounds against infections in various parts of the body, the report emphasises once more the importance of beginning the treatment of acute infections with a large initial or loading dose—which in severe cases may have to be intravenous or intramuscular In severe infections the concentration of sulphonamide in the patient's blood should be ascertained if possible about 12 hours after beginning treatment, and again at 24–36 hours, for absorption from the alimentary tract is variable and there are other uncontrollable factors The total dosage of sulphonamide (midnight to midnight) should be recorded on the temperature chart each day, and doses should be ordered and recorded in grammes not tablets, for the content of tablets varies (The seventh addendum to the *British Pharmacopœia* requires the dispenser to issue 0·5 g tablets when sulphanilamide, sulphapyridine, sulphathiazole sulphadiazine, or sulphaguanidine tablets are prescribed without mention of the strength)

The section on toxic and other harmful effects will be of special value to anyone who being confused by the complexities of this subject, is inclined unjustifiably to trust to luck The first step should be to find out whether the patient has ever had sulphonamide before and (if so) in what dosage and with what effects

"A patient who has had a toxic reaction to one of the sulphonamide group of drugs may have a second and more severe reaction if any of these drugs is prescribed again on the other hand it is possible for a patient to be sensitised by a first course of sulphonamide without showing any symptoms until one of these drugs is again administered Hypersensitivity to one compound often but by no means always—implies hypersensitivity to other sulphonamides Where the clinical condition permits of delay in beginning therapy, it is advisable in such individuals to give a small test dose of the drug (0·1 to 0 3 g) 12 hours before the main course of treatment is started; the patient

1 Medical Research Council War Memorandum No 10 2nd ed 1944 Stationery Office, 1945 Pp 71 1s 3d
2 See for example Babel in the Drug Trade *Lancet* 1943 ii 195.

should be carefully observed thereafter, and the drug immediately stopped on the first appearance of any toxic manifestation"

"Patients taking sulphonamides in therapeutic doses ought, when possible, to be seen by the doctor at least once a day" so that he may inquire into such early toxic symptoms as headache, nausea, vomiting, and malaise, and such signs as cyanosis, rashes, jaundiced scleras, or pale mucous membranes The temperature must be recorded, and the report gives valuable advice on drug fever, as well as granulopenia and urinary complications—their recognition and avoidance These and other ill effects, including rashes, may be attributable to hypersensitivity,[3] and methods of desensitisation are briefly considered As a rule sensitisation is not apparent until the drug has been taken for about 8 days, and sulphonamide therapy should rarely be continued for more than 7 days Use of these drugs over a long period, in small doses, may be permissible to prevent relapses in so serious a disease as rheumatic fever, but their continuous administration over many months to the members of a community—such as a factory—to protect them from respiratory infections "is not at present to be generally recommended" Where, on the other hand, an outbreak (e g, cerebrospinal fever or bacillary dysentery) can be controlled by small doses given for only a few days, chemoprophylaxis may be clearly justified American experience in the prevention of gonorrhœa and chancroid is quoted without comment.

As for the future, "the spheres of sulphonamide and penicillin treatment overlap to a large extent, but penicillin is usually the more efficient remedy in conditions susceptible to both" and "when supplies permit it will replace sulphonamides more frequently In a few infections penicillin has a therapeutic action and sulphonamides have none, in others (e g, bacillary dysentery) the sulphonamides are more efficient than penicillin" The relative advantages and indications are briefly explained in the report, which points out that for local application penicillin is superior because of "its efficacy against even large numbers of bacteria," because nothing in inflammatory exudates antagonises it and because it is almost non-toxic to tissues

POLIOMYELITIS IN EUROPE

A SERIOUS outbreak of poliomyelitis which began in Belgium at the end of May[4] appears to have reached its peak during August The total number of cases up to Aug 19 was estimated at 800–900, actually 750 cases were notified, but this figure is unreliable because at first many of the cases were not reported, while later many were notified on a misdiagnosis According to a revised record by the Ministry of Health, a total of 554 known cases was reported up to Sept 1 Of these, 165 occurred in West Flanders, 106 in the Liége Province, and 101 in the Brabant In Western Flanders, where sporadic cases were reported in May and June, the incidence increased appreciably during the first fortnight of July, when the disease appeared also in epidemic form in the province of Liége at Verviers and in the Brussels area, Antwerp was affected in August

The disease seems to be of a particularly severe and rapid type, bulbar paralysis being common and early, the fatality-rate at first was given as 25%, and at the middle of August it was 15% All age-groups have been attacked, and many people died within 48 hours of the onset, a few within 24 hours Means of spread have been hard to trace, but the summer has been dry and flies abundant. During the last week of August the disease was reported throughout the country, with numbers of cases still high in the Brabant (Brussels) and West Flanders The infection was further spreading towards Holland into the Dutch Limbourg and into Germany via Eupen and Malmedy. The Grand Duchy of Luxembourg, according to reports available up to the end of August, had apparently escaped infection

We have no further news of the outbreak in Prague, where about 100 cases had been reported by Sept 8, and thereafter about 6 cases daily Epidemics were also reported in Sweden, Finland, and Denmark early in September

CHARLES SPEARMAN

Prof C E Spearman, who died on Sept 17, was of the spiritual progeny of Galton He applied mathematical procedures to psychological phenomena, and moulded the outcome of his analysis into a theory which has greatly influenced modern psychology Nurtured in Wundt's laboratory, he valued accuracy of observation and tidiness of experiment far higher than speculative ingenuity, but he was bold in developing theory so that it would be in keeping with his findings His two notable works on *The Abilities of Man* and *The Nature of Intelligence* gave him a permanent place in the history of psychology—the subject which he himself brilliantly and critically expounded in his last work *Psychology down the Ages*. His studies of individual differences did not stop short at measurement and discrimination, but led him to formulate a theory of mental structure which still exercises great influence The statistical method of which he was a pioneer has now entered into its kingdom here and in America.

Spearman was always anxious that the methods he had developed should be applied in psychiatry He urged this cogently in his Maudsley lecture to the Royal Medico-Psychological Association, but in spite of some contributions made on these lines by pupils and collaborators of his, the development of factorial analysis as an instrument of psychiatric research has followed lines somewhat different from those which he conceived Nevertheless his indirect influence upon psychiatry has been considerable

A CHAIR OF ANATOMY

ON another page we announce the appointment of Mr. J Z Young, FRS, a zoologist, to the chair of anatomy at University College, London. "Tradition in this department," writes a correspondent, "favours a broad conception of the field of anatomy, which is thus likely to be continued Professor Young's work before the war on the nervous system of many species, and his fruitful collaboration with clinical colleagues on the Nerve Injuries Committee of the Medical Research Council during the war, suggests, further, that the especial emphasis on neurological anatomy associated with the work of Elliott Smith and Woollard at University College is to be maintained Experience gleaned in unusual fields should enable him to bring fresh ideas to the current reconsideration of preclinical training, and to the teaching of anatomy itself"

A NEW DIPLOMA

THE Society of Apothecaries of London has decided to institute a diploma in industrial health Particulars will be found in our news columns

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ON Thursday, Oct 11, at 5 PM, Sir HOWARD FLOREY, FRS, will deliver the Lister lecture at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, WC2 He will speak on the use of micro-organisms for therapeutic purposes

Sir WILLIAM DOUGLAS, KCB, permanent secretary of the Ministry of Supply since 1942, has now taken up his duties as permanent secretary of the Ministry of Health on the retirement of Sir John Maude, KCB

3 See *Lancet* Sept 22, p 374
4 Unpublished *Bull Communicable Diseases and Medical Notes* Sept. 5, 1945, p 42

Reconstruction

BETTER HOSPITAL SERVICES

SOME LESSONS FROM THE SURVEYS

(FROM A CORRESPONDENT)

THE reports of the surveyors whose duty it was to examine the existing hospital provision throughout the country are now being published Most of the short comings had been proclaimed by the profession itself before ever the surveys were announced. But now we have a fair sample of the facts

Unfortunately a blue book is a formidable document. Presented with a dozen in succession the most voracious reader may well fear for his digestion and abstain

Administrative action can alter the existing organisation, but its contribution to improvement will be largely material and long term To the immediate task of integrating our existing resources the members of the profession itself must, it seems to me bend their energies The difficulties before us have their roots far back in time, and it can do no harm to reconsider the background against which we have to work It may make the surrender of some of our prejudices—for we all have them—a little easier The background is clear enough for most of the country save the Metropolis The multiplicity of activities in the foreground tends to confuse the Londoner s view

THE "VOLUNTARY SYSTEM"

The voluntary hospitals were founded, often endowed, and for more than a hundred years have been supported upon compassionate grounds Local pride is as old as local settlement, and localities are proud of their territorial hospitals In very many instances the pride is justified, but the self-sufficiency to which it leads is an anachronism It was from the leading voluntary hospitals that the whole structure of modern British medicine was built up It was on the basis of their progress that the municipal and county hospital system became possible They have produced the staffs to do the work of the publicly provided hospitals

The basis of financial support for the voluntary hospitals had slowly and steadily widened until after the last war the beneficiaries themselves began to take a hand, and did so with such determination that the system, which seemed threatened with failure, obtained a new lease of life from contributory schemes The success of contributory schemes arises however only in small part from the benevolent urge which had for long years lain behind hospital contributions The contributors had become used to "insurance" of many kinds, and the "penny a week" appealed to them in that guise *It fortified their pride in their local hospital* by adding a conviction that here at need, they would get the return for their money The managements of hospitals have not always realised that what they asked for as freewill offerings was nevertheless given with a quick sense of quid pro quo Nor have they advertised the terms, somewhat belatedly acclaimed upon which they meet their contributors It was naturally taken for granted by them, since it had become established practice, that the quid pro quo would be the treatment of acute illness only, with a limit of thirteen weeks Moreover the voluntary managements did not foresee that the number of contributors would become so great as to exceed their resources in beds and services *It is by* no means impossible that "contributory schemes" would in the end have rung the death knell of the voluntary principle

RIVALRIES

The appropriated hospitals, taken over by local authorities under the Act of 1929, had a bad start They had to live down the unhappy reputation of poor law institutions—the slur of the workhouse—and generally had to do it in, or associated with, the very unsatisfactory buildings surrounding the "casual wards" The great efforts made by many local authorities to surmount their difficulties and defeat their handicap are still imperfectly known to, or appreciated by, the voluntary hospitals

Rightly or wrongly, the local authorities set to work first on material improvements, equipment and buildings, though the standard of staffing was considerably raised, full development was temporarily postponed At the moment when the staffing problem was exercising the minds of local authorities anew, the war came Yet in many places great progress had been made and has continued throughout the last five years, receiving considerable impetus from the Emergency Medical Service dispersal of patients and staff

Some members of health committees of local authorities seem frankly to detest the voluntary hospitals and all their ways They resent the persistence of the notion of "charity" The replacement of benevolence by insurance, which underlies the contributory schemes annoys them because it disarms one of their attacks upon voluntary bodies With the capacity to outbuild and out-equip their rivals, they have so far won less popular confidence than they feel they had a right to expect Here and there they have succeeded admirably and there it little doubt that, continuing on their present lines, they could in time win an equal, a *numerically superior*, and ultimately a *leading place in the hospital situation* They are, however, not unnaturally, impatient of slow progress Some of them want to destroy or absorb the rival system and as elected representatives of ratepayers, reign supreme in control of all hospitals It does not temper their claims to exclusive dominance that "election" takes place on political grounds, or that health committees generally speaking have but limited qualifications in expert knowledge of medical science and in contrast to comparable voluntary hospital committees, have no *body* of expert advice at their disposal.

There is a good deal to be said on the side of the health committees The word 'voluntary' is ceasing to have its old meaning It still denotes the status of the management committees, but the paid administrative officers are now much more numerous than formerly and (without much public announcement) payment of the doctors in some form and in some degree has gradually modified the purely voluntary status of the 'honorary' medical staff The tendency is most obvious where contributory schemes are most active and successful, but in one respect it touches almost all voluntary hospitals—namely in the increasing number and age of the resident and junior staff who are paid

It has always been recognised that the voluntary service of the honorary staff of voluntary hospitals is rendered in the hope, generally but not always successful, that the reputation gained will bring material reward from a private clientele but there is a suspicion in the minds of some members of health committees and local authorities that in the smaller general hospitals the staff regard the hospital as a remunerative element in the services they can offer their private patients in whose interests they are thought to exploit its resources Here and there there is some reason to think the suspicion justified, but it is not entirely a witness to sordid motives. It is an undeniable fact that the best family doctors (that is, the doctors who give the best service) feel acutely the need of hospital service at their own disposal if they are to do well by "their" patients

It has been argued that there should be no 'their' in the doctor patient relationship but that cuts at the root of the principle of personal responsibility which is the basis of good treatment That good doctors use their hospital privileges for the patients towards whom they feel responsibility because of the fees received even

to the exclusion of others whom they do not know, is really an argument for provision of the same hospital resources for all doctors, and for the evocation of the same sense of personal responsibility in all doctors It is not wholly a reproach even to those doctors who, feeling and implementing their responsibility, also correlate it with the financial reward that good service deserves.

Nevertheless, concentration upon monetary interest if it be blatant, elicits contemptuous condemnation from those entitled to throw stones.

ACHIEVEMENTS OF THE TWO SYSTEMS

In the few instances where the local authorities have erected well-planned modern institutions, both well-equipped and adequately staffed, they have produced hospitals, or clinical units, which are as good as their best voluntary counterparts Very few completely modern voluntary hospitals or units have been built, and in many equipment is less good than it should be, because of its great expense Moreover, the staffs of some voluntary hospitals are not fully trained for the special work they undertake, nor is it adequately supervised by the consultants and experts in the various branches of medicine. In some places there is local knowledge of this defect and it minimises the repute of the voluntary hospitals

In two respects, however, the voluntary hospitals have hitherto been able to claim an advantage The first is that they know no boundaries, their patients can and do come from as far afield as transport makes convenient No person is excluded because he lives on the wrong side of a line marking parish or district bounds Latterly, though the principle remains, this extremely important freedom has been rather spoilt by obligations to contributors Territorial restrictions upon the right of admission to local-authority hospitals are an impediment to equality of service for the rural and urban populations

The second advantage is the provision of outpatient departments, which until recently very few if any rate-supported hospitals furnished To this distinction is largely due the tendency of the "best" cases to get into voluntary hospitals, but in many places it is now countered by the comparative ease with which practitioners can secure beds for their acute and emergency cases in rate supported hospitals

The local authorities have a monopoly of infectious-disease hospitals Some are very good, some pass muster, but not a few do little credit to those responsible for them. They are staffed with difficulty and many are out of date in construction Provision for smallpox is often pitiably wretched Many of the small sanatoria are but poor advertisements for small local authorities as health authorities The conditions in which all types of chronic sick are housed ("herded" would be a more accurate term) are in many instances a blot upon the social conscience, and a reproach alike to the voluntary-authorities who have disclaimed any responsibilities in the matter, and upon the local authorities who have been unable to escape an obligation

BUILDINGS AND SITES

Hospital buildings, with relatively few exceptions, are not satisfactory. Many, particularly of the voluntary hospitals, were well adapted, *when built*, to the recognised requirements of hospital treatment at that date; but not a great many have been erected in this century Modern designs differ materially from those proper to the purposes of fifty years since Where praiseworthy attempts have been made to keep pace with changing demand—and that is almost everywhere—the result has been threefold aggregations of buildings upon an uncoördinated plan, unsatisfactory and make-shift adaptation; disappearance of the open space around the original building

In the case of municipal and county hospitals, "appropriation," generally speaking, has meant the conversion to hospital uses of buildings erected under the poor-law, some of them on the common plan of 1836 Most buildings now used are of much later date and of very much better design, a few are modern, at any rate as to some pavilions or units, and in that case the plan is good, although the "slump" of the early 'thirties led too often to spoiling the ship for a ha'porth of tar

In most of the county boroughs the only entirely satisfactory recommendation involves the construction of a new general hospital, and the scrapping or diversion to another purpose of existing hospitals In almost any given county borough an outsider entirely free from local pride and prejudice would come to the conclusion that the best hospital service could be provided for the people by a combination of existing resources, and nearly always by scrapping all existing buildings and erecting one, or at most two, new buildings on a better site. Where town-planning would permit of the erection of the new hospital on a site with really wide open spaces around it, in the town, there are advantages in a central site As a rule a suitable situation is to be found on the periphery, and something like 50–100 acres is not excessive

There is nothing against, and much in favour of, diversity of method in carrying out the fundamental plan In one town, where circumstances are favourable, everything might be concentrated upon one peripheral site and the public transport be adapted to the distance —ambulances, buses, service lorries, and in a little time hence, a local airport In another place the geographical conditions may dictate the provision of two hospitals at the extremes of its boundaries In either case it may be wise, or even imperative, to maintain an out-patient and casualty department, and even an emergency operation unit, in the industrial centre

The new hospital buildings, however grouped or dispersed, should be strategically placed with the full coöperation and advice of the town-planning authority Since it is to be feared that for some time to come hospital building may have to give way to other priorities, it is of the utmost importance that town-planning should look far ahead, not only for the siting of the hospital, but also for sewers, water and other services, roads, transport, and vehicle garages and depots In the meantime a rigid control should be exercised over expenditure on expansion and reconstruction programmes of all existing hospitals If priority for such work can be obtained, it can be obtained for the erection of corresponding items in the future hospital plan, which should be implemented as often as occasion offers

FUSION AND DIFFUSION OF STAFF

Material fusion is, unhappily, doomed to postponement because of the priority justly claimed by "housing" It remains to examine the possibilities of fusion and diffusion of staff

The motor-car has made it possible for the many able and experienced specialists—physicians, surgeons, gynæcologists, pathologists, and others—to visit places many miles from their residences A great deal of diffusion of specialist service is already afforded by periodic visits of consultants from central to outlying hospitals, from the teaching hospitals to the voluntary hospitals in distant towns, from those hospitals to smaller and "cottage" hospitals, and from voluntary hospitals to municipal and county hospitals

There are, however, serious defects in the existing system It is alleged that visits are often too widely spaced, are too often perfunctory, and in some places may occur only when a fee-paying patient warrants a journey It is stated that the numerous names of visiting consultants listed in the annual reports of peripheral voluntary hospitals are sometimes mere camouflage—as for example, when the consultant in question

lives in London and purports to serve a hospital 200 miles away It is asserted, and indeed freely acknowledged in some cases, that the consultants and specialists attend only "on request" to see a particular case, and that although there may be a case in each adjoining bed equally in need of advice or treatment, the visitor has no right to tender his help to them

There is a further criticism of serious importance Major surgery is often done by visiting surgical specialists in hospitals distant from their place of residence, where they lack the special resources of their own theatres, laboratories, and technical departments Their patients are deprived of their personal daily observation and treatment, a serious disadvantage even where no complication arises In the case of "cottage" hospitals, moreover, there are no resident doctors Similarly though perhaps less dramatically, the absence of the consultant physician during the stages of acute or serious illness deprives patients of the very best chances It seems essential then that to bring the fullest value of expert skill to patients in the outlying towns and districts, the consultants, or many of them, must be domiciled at or near the site of their chief responsibilities

Some of the implications of the dispersal of domicile involved may be suggested If a man has teaching duties in a medical school and is expected to live elsewhere than in the university city, those duties should be so arranged as to permit their performance by visits They might be limited as to duration within so many weeks or months per annum, they might indeed be totally diminished, as would be possible if teaching were in the hands of whole time educational experts—the university professors, their readers and assistants—while the rest of the "honorary" staff took a minor share, or a more particularly apprentice" type of clinical instruction On the other hand, if from the specialist units and departments of the "teaching" and associated hospitals, the chief assistants were regularly seconded to outlying hospitals, it might well prove possible for members of the professorial staff who had trained those men, to give in a much shortened time, the amount of advice and help which now demands more prolonged absence than is permissible if their central responsibilities are to be satisfied

MALDISTRIBUTION OF SKILL

There are several established area services which are spread over the countryside and yet manned by those living in the cities Nevertheless, outside the metropolitan areas it is a constant complaint that by no means all who need the highest skill can or do obtain it It is alleged with some justification that the highest skill of a physician is lacking in many towns as well as in the *rural parts; that surgery is done by those who, neither* by the equipment at their disposal nor by training nor by availing themselves of opportunities for keeping up to modern standards are fitted to perform all the work they do There are districts in which high gynaecological and obstetric skill is at the disposal of all, there are many where it is not There are, here and there, good laryngological and ophthalmological services but by no means every hospital, nor every patient receives fully all that is needed Excellent as are the centres for the rarer specialities, it is by no means the case that all who might profit find their path to them as easily as might be, nor are they encouraged to overcome their natural reluctance to travel far from home and brave the unknown, by a full relation of the advantages—often life saving, or at least preservative of wage-earning capacity—that a journey to the centres would afford There is a widespread feeling that whatever may be lacking and need to be supplemented, the best is not being made of the assets at hand

Staffing defects can be traced very largely to an economic factor The great majority of doctors entered a profession established time-out-of-mind on a fee earning basis A great deal of medical work has been, and is still being done (though perhaps in less degree), without expectation of any monetary reward; yet the law of supply and demand governs the earnings of doctors and, as in other professions and occupations, exceptional skill, an exceptional personality and business ability secure lucrative reward Whilst some specialists make fortunes, many do little more than pay their way, and not a few leave their widows little better than destitute Money is most easily made in cities and large towns Most specialists cannot make a living in small towns or in rural areas

Another consideration plays an important part, the education of the doctors children All doctors want *good schools for their children and when the children* are young they want the schools within easy reach So even if a good living could be made in a small town or in a wholly industrial area young specialists and almost all ambitious family doctors prefer to practise where good educational facilities exist If they cannot start in such a place they seek an early opportunity to move thither

Still another weighty influence on the residential distribution of specialists is the simple fact that the hospitals and laboratories which alone enable them to do their work properly are, generally speaking better and more fully provided in the larger and richer towns The same, of course, is reached where there is a university

EXAMPLES OF BETTER DISTRIBUTION

Before the war the foundations of some area services were firmly laid The powers of the Emergency Medical Service have been instrumental in establishing other examples of distributed skill The blood transfusion organisation has been responsible not only for greatly improved treatment, but for the dissemination of information, for widespread instruction, and for the furtherance of coöperation with the universities The Emergency Pathological Laboratories have brought essential resources to some places where none formerly existed; have improved those of others beyond recognition and have strengthened all Not the least of many gains has been the recognition by a university of the heads of area laboratories in its sphere as associated members of the university department of pathology

In the last few years the major specialities—neurosurgery, thoracic surgery, plastic (maxillofacial) surgery, orthopaedics and radiotherapy—have been established in a few centres throughout the country, in the university cities generally, in or associated with the teaching hospitals and under the control of the leading consultants of the day The Emergency Medical Service has thrown *them into prominence partly by increasing their accommodation* by providing special units in hospitals away from the target cities, by providing transport for segregation of cases, and by supplementing the staffs The Emergency Medical Service has also added others for neurosis, effort syndrome and rehabilitation It is true that war casualties have provided a large proportion of the patients of the surgical units but the existence of the facilities has quickly demonstrated both the need for such units for the civilian population and the conditions requisite for their satisfactory establishment

The staff required must be extremely highly trained This applies to the nursing technician and secretarial personnel as well as the medical The number of junior staff needed is high The equipment must be comprehensive and of exceptional quality The provision of convalescent' or 'long-stay' beds in hospitals must be generous. On the other hand in peace the number of cases calling for treatment is of such an order that not many of these units are necessary In the future every major "region"—that is the sphere of influence of every university city, and perhaps two or three others—should have such units It is important that the staffs should

have full experience, and for that purpose, as well as for the obvious benefit of the patient, all cases from a region should be segregated, though in special circumstances it may be convenient for a unit in another region to be chosen for some particular person

Where physicians or surgeons of exceptional skill and experience are found in hospitals other than those housing a special unit it should rather be for them to be attached to the unit than for cases to be retained in or directed to their clinics Eventually it may be found convenient for them as members of the staff of the special unit, to do some of the work, in consultation with the chief of the unit team, in their own clinics, but a multiplicity of units is at present undesirable

The Emergency Medical Service hospitals established in mental and other county and municipal hospitals and in public-assistance institutions, many of them remote from towns, have been staffed by young and highly trained men, who have found full scope for their abilities, have set up really good units, and done admirable work, but they are in these outlying places, it must be remembered, because their movements are controlled and because the State pays their salaries To these last hospitals many consultants have been attached and have received remuneration for their services Some have paid regular and frequent visits; others have visited irregularly or on call In almost every case, when urgent or numerically arduous work called, the service was forthcoming

The distributed services should leave no enclave within the territorial limits of any scheme, and the future health authority will presumably eliminate such a possibility

The Emergency Pathological Service has overcome a great many local objections because financial assistance and help with the provision of trained staff have been forthcoming, in the provision of other area services the same lever will be needed to ensure coöperation

UNIVERSITY INFLUENCE

The "sphere of influence" of a university is often defined by the extent of its educational, forestry, veterinary, or specifically industrial faculties Such spheres are found to have, within their geographical borders, areas centred upon towns towards which roads, railways, and therefore marketing interests, naturally flow They are generally the catchment areas for patients in voluntary hospitals Presumably a university city will always attract the exceptionally able man, and the exceptional services will be centred there, but broadly speaking it should be for the university of an area, not only to put the stamp of its approval on a specialist's examinational standard at the outset of his career, but to lay upon him, wherever in its sphere the man may be working, the obligation which educational responsibilities entail, of keeping the standard of his performance up to current university level

There are various ways in which the distribution of skill to extra-university hospitals might be secured

(1) The usual house-appointments of qualified and "registered" men who would lose no priority or rights as regards higher appointments by their "seconding" to non-teaching hospitals It is probably inevitable that the best men would try for appointments in teaching hospitals, but it is not impossible to offer other men compensating advantages

(2) The appointment in "district" hospitals of resident surgical officers resident medical (physician) officers, registrars, and chief assistants who would have somewhat greater responsibilities than in the parent hospitals and would thus have the opportunity of proving their work and fitness for higher office as full members of the staff of another area or even of a teaching hospital The dean or professor of the university, in liaison with the local service staff, should keep them under his eye They should be encouraged to keep in touch with the teaching centre

(3) The use of members of the staffs of teaching and other great hospitals, who already tend to live 15–30 miles out from the city's centre, as additional consulting members of some district hospitals They can be induced so to do with certainty, at present, if the hospital has good private wards, and when services are paid for, or when the principle of an "area service" is introduced, they can be allotted such duties

(4) There is the possibility, of which some examples can be furnished today, that senior men on retirement from their teaching hospitals can still give five years of very valuable service to the hospital in the neighbourhood of their retirement domicile. Their experience and prestige secure the men themselves against jealousy, and are a great advantage to the hospital

(5) If it became a part of the General Medical Council regulations that students, after qualification, serve as residents for a year before "registration," the licensing bodies, particularly the universities, would of necessity use a great many hospitals, which they would have to "inspect" before entrusting them with a most important year of the students' education

It will be important, when men are stationed at a distance from a university, to make clear that they are only "seconded," and that, far from imperilling their chances of promotion in the teaching unit, the additional responsibility entailed by conducting work beyond the range of constant supervision by their superiors affords opportunity for proving their general capabilities as well as their professional competence

THE PRIVILEGE OF TEACHING

"Partnership" between the local authority and the voluntary hospital systems will not be effective or vital without a generous pooling of assets

The most valuable asset on the voluntary hospital side is their virtual monopoly of the production of doctors Admitting that in the last ten years the schools have called upon the "patient" resources of rate-aided hospitals to supplement their teaching material, and that recently one or two chairs have had their locus in local-authority hospitals, admitting too the success of the British Post-Graduate Medical School of the London County Council and the University of London, yet by and large it is true that undergraduate medical education is in the hands of the voluntary hospitals

The most striking difference between the two systems is that the one is staffed by men whose major contacts with patients are outside the hospital—if not actually in their homes, at least in the course of their daily lives, and in association with those whose practice is in and among the family The local-authority hospitals are staffed by whole-time officers, the whole of whose duties are within the walls of the hospital

So far as the work within a hospital is concerned, there is little doubt that it is better performed by whole-time officers, but, important as the hospital work may be, it is only a part of the service of curative medicine needed by the public, and it is imperative that all those who practise outside hospitals should, for the maintenance of the standard of their work, have opportunity, within the hospital, of extent corresponding to the character of their special functions

In the opinion of many of those who have experience of both services, it is essential, if the best use is to be made of the opportunities open to local authorities, that the system of staffing at present in vogue in local authority hospitals should be modified, and modified much in the direction of the long and well-tried system usual in the voluntary hospitals Demands for change in local authority hospitals and for the acceptance of change by local-authority committees will be made and no doubt resisted The point seems to me fundamental, and the quid-pro quo that seems to me most appropriate

is the surrender by the voluntary hospitals of a claim to monopolise undergraduate teaching

There is another point—psychological perhaps and of diminishing importance—that the staffs of local authority hospitals say they are conscious of ranking lower in public esteem than their colleagues on voluntary hospitals If the municipal hospitals had a share in the production of doctors there would be an equality at the top where the highest posts in academic standing would be open to their staff, and the equality of opportunity through the lower ranks would eliminate the very undesirable sense of inferiority of status

Wherever the teaching hospital has a long tradition behind it it would be foolish to sacrifice that even nominally, but in the one or two places where new teaching schools are needed it would be sensible, whilst incorporating from existing voluntary hospitals everything locally available to establish one or more of them in local authority hospitals Still more important would be a gesture by the university, at any place in the country where the situation offers a likely chance of success, suggesting joint effort in the establishment of a new combined municipal and voluntary teaching hospital The university is the most likely body to succeed in bringing the parties together and establishing itself as an impartial authority Whilst accepting a very important obligation, it would not be inviting a burden, for neither finance nor administration need be imposed on the university authorities

A great deal of attention is being directed to "postgraduate" university teaching It is not always appreciated that postgraduate education includes, first and foremost, the training of all the whole time young residents, registrars, and chief assistants and that it is the duty of their "chiefs" to give time and energy to that end. In other words, a most important share in the education of practitioners and specialists is taken by the staffs of the largest non teaching hospitals Their educational work has hitherto received little or no recognition; but if the universities, through their medical faculties, extend their interest to seconded men the value of the posts in non teaching hospitals will rapidly rise, better men will be attracted, and the degree of skill permanently at the service of outlying populations will be raised

Special Articles

THE PILGRIMAGE TO MECCA

MEDICAL CARE OF PILGRIMS FROM THE SUDAN

E N CORBYN

FORMERLY GOVERNOR OF KHARTOUM

It is the religious duty of a devout Mohammedan to make, once in his life time, if he has the means the pilgrimage to Mecca either personally or by substitute Therefore as there are many devout Mohammedans in Africa, there has always been a stream of pilgrims, from West Africa Nigeria the Lake Chad regions and the Anglo Egyptian Sudan converging at the time of pilgrimage each year upon the Red Sea coast for transshipment to Arabia Many from the distant countries making the journey on foot and stopping for periods at places where work can be found to give them the wherewithal to start upon the next stage may take two years to go, and two years more to return home with the proud title of *El Haj*—one who has made the pilgrimage Each year therefore brings a mass of varied humanity to the starting point for the Arabian pilgrim port of Jedda This traffic has been canalised by the Sudan through its own port of Suakin

The pilgrimage from Suakin through Jedda to Mecca vitally concerns the health authorities of the Sudan in two ways—the protection of the health of pilgrims from the Sudan while on the pilgrimage and the protection of the Sudan from the introduction of diseases by returning pilgrims

All who go upon this pilgrimage must of course be Moslems, members of Islam, the Mohammedan religion Unless therefore there are trained doctors who are Moslems to go with them, medical protection cannot be given to the pilgrims It is here that the Sudan pilgrims have now begun to reap the benefits of the foundation in 1924 of the Kitchener School of Medicine in Khartoum Trained Sudanese doctors of Moslem religion have been produced by this school since 1928, and are now spread into all public health services of the Sudan

In 1942 for the first time a Sudanese doctor accompanied the pilgrims to Mecca and Medina By 1944 the experience gained had enabled a much larger and more satisfactory medical mission to be planned

The medical mission which went with the Sudan pilgrims in 1944 consisted of two qualified Sudanese doctors, a medical assistant, a sanitary overseer, and a hospital staff of six male and one female attendants, a cook, a storekeeper, and two motor vehicles equipped to carry stretchers, with their drivers A tented hospital of 30 beds was erected two miles outside the port of Jedda on the Mecca road, where one doctor and the majority of the staff were stationed At Mecca was a dispensary under the charge of the medical assistant At Medina was the other doctor with a dispensary with five beds.

At the peak of the religious celebrations which culminate at Mecca and at Arafat a day's march away, the whole staff was concentrated there to afford the maximum of medical and sanitary facilities for the Sudan pilgrims Hospital cases were passed down to Jedda and, if necessary, straight across the Red Sea to Suakin on returning ships Although inpatient treatment in hospital was restricted to Sudanese pilgrims, outpatient treatment was given to all who asked for it, in accordance with the tradition of medicine and in the spirit of the pilgrimage More than half the outpatient attendances were of other than Sudan pilgrims The hospital at Jedda has been dealing with about 3000 outpatients a month in addition to inpatients, and the dispensary at Medina with about 8000 attendances a month; and during the two weeks when the whole medical mission was concentrated at Mecca and Arafat there were about 4000 outpatient attendances The hospital at Jedda is very popular and its outpatient facilities are used by the people in all walks of life official and non-official, and by patients of many races

The Sudanese pilgrims, who in 1944 numbered 6999 out of a total of 96 000 pilgrims were most appreciative and enthusiastic about the work of the medical mission in providing adequate medical facilities for them at all stages of their journey, and in protecting their health by sanitary precautions particularly at Mina between Mecca and Arafat and other places where there is most danger of epidemic disease. There was no quarantine disease among the Sudanese pilgrims The only deaths which have occurred in hospital were two from pneumonia, which cannot be completely avoided during the rainy season in the Hejaz, and the deaths were reduced to this number by the availability of treatment with sulphonamide drugs The state of health of the pilgrims as a whole was most satisfactory throughout the pilgrimage

The careful supervision of the pilgrims almost eliminated the risk from smallpox and as a result the period of quarantine at Suakin on return was reduced to three days only compared with eight to fourteen days in previous years This was greatly appreciated by the pilgrims

A special transit camp has been built at Suakin for the accommodation of pilgrims on the outward journey, and it has made their stay at Suakin much more comfortable and has facilitated the medical arrangements at that stage of their journey

The cost of the medical mission to Sudan taxpayers is over £5000 a season and it was important to ascertain whether the expenditure was justified Accordingly the British director of the Sudan Medical Service visited Jedda, and on careful inspection his findings were most satisfactory The Sudan pilgrims have now a complete medical and health organisation at their disposal throughout their journey, and the arrangements are as effective as can be devised to ensure that they are detained for the minimum period in quarantine on their return The benefits to the health and comfort of the pilgrims, and to the public health, amply justify the cost to the taxpayers. The results reflect most favourably on the Sudanese doctors and personnel, who are administering an efficient medical and health organisation which is bringing great credit to the Sudan in Arabia The Sudan medical mission has been much indebted also to the British Legation at Jedda for assistance and guidance at all times, and to the officials of the Sa'udian Government for their sympathetic coöperation and help

RHEUMATISM

A SCHEME FOR SCOTLAND

IN Scotland in 1937–38 (the last year for which we have detailed figures) rheumatic disorders were responsible for 45,000 fresh incapacities, and for the loss of 3 million working days The rheumatism subcommittee of the Medical Advisory Committee (Scotland) have therefore good reason for saying [1] that the cost to the nation is large enough to make rheumatism a major problem. They have confined their study to chronic rheumatism, in which they recognise an articular group (rheumatoid and osteoarthritic types) and a non-articular (muscular and neuritic types) A survey in Aberdeenshire showed that almost 10% of all the work done by general practitioners was concerned with the diagnosis and treatment of rheumatic conditions, the great bulk of the cases being muscular and neuritic

Existing facilities for treatment are agreed to be incomplete Most patients could benefit from some form of physiotherapy, and the private doctor can give this only if he has the necessary equipment People referred to hospital are usually treated as outpatients, and given a course of physiotherapy, often without preliminary X-ray investigation Treatment depends on staff and equipment, the pressure on the physiotherapy department, and the patient's ability to attend There are three large clinics, at Edinburgh, Glasgow, and Dundee, and one or two small ones have lately been opened in Glasgow and elsewhere The chief Glasgow clinic gives some domiciliary treatment to bedridden patients, and a mobile physiotherapy unit is under consideration All three main clinics are unsuitably housed the Edinburgh clinic is in a terrace house which is not large enough; the Glasgow clinic is in an adapted church, again too small, and the Dundee clinic is in a converted factory, which is satisfactory in some ways, but (like the other two) has too many stairs

Many of those giving evidence to the subcommittee held that clinical investigation at the outset is often inadequate, and that physiotherapy is often given as a routine, and for too long a time without critical clinical assessment Accommodation for both inpatient and outpatient treatment is insufficient, and it is believed that the period of disability could be shortened for many patients if they could be treated as inpatients Doctors who have made a close study of the treatment of rheumatism are scarce Though little may be known of the causes of rheumatism, a reasonably accurate diagnosis is possible, and the various types can be distinguished at a fully equipped hospital or clinic The subcommittee emphasise that X-ray examinations should be made early, and in far more cases than is now usual Experience has shown that treatment can alleviate pain, lessen the chance of deformity, and cut short the time of disablement The general practitioner, though often able to treat the acute stage successfully, usually has not the means at hand to treat the chronic case In rheumatoid arthritis "no known remedy can be relied on to arrest the joint lesions" as the report says, the outlook for these patients, when treated at home, is gloomy

The subcommittee recommend the provision of hospital facilities for the investigation of every case of articular rheumatism, to establish the diagnosis and determine the appropriate treatment If inpatient treatment is needed the patient should be admitted, and throughout treatment, whether as inpatient or outpatient, he should be under direct and continuous medical supervision They point out that research is urgently required to assess the value of every current form of treatment—including diet, drugs, and bacterial and immunological products—and to seek new and more effective remedies Instructions to physiotherapists should be exact, and care should be taken to treat the patient, not the disease. Physiotherapists must be encouraged to lay more emphasis on active exercises, and passive therapy should early give place to active movement and a progressive course of exercises The physiotherapy department of a hospital should be supervised by an experienced physician or orthopædic surgeon who will review each case frequently Medical students, the subcommittee suggest, should be taught the principles of physical medicine, and postgraduate courses should be arranged for general practitioners Occupational therapy can be beneficial in suitable cases They take a practical view of hydrotherapy as a useful adjunct to other forms of treatment, but are little impressed by the special advantages of the waters at various spas Patients needing lengthy inpatient treatment might, they think, be admitted to long-term units to be set up in selected large hospitals, and they propose that in at least one hospital affiliated to each of the four universities 20–40 beds should be reserved as a central unit for the intensive study of chronic rheumatism, beginning with the articular types The long-term units should not, however, deal with incurable cases, which should be referred to centres for the care of the infirm

Peripheral clinics, it is thought, should be established on modest lines for the present, and should be linked with the existing orthopædic clinics, and with the long-term hospital units Follow-up of patients discharged from hospital should be carried out through the clinics, which could be placed under the charge of a local general practitioner in each area provided the specialists at the central units paid regular visits to them

[1] Chronic Rheumatic Diseases Edinburgh HM Stationery Office Pp 25 6d. The members of the subcommittee are Sir John Fraser FRCS (chairman), Sir Alexander Macgregor, FRFPS, Prof Adam Patrick, FRCP, Dr D Dale Logan and Dr A F Wilkie Millar, with Dr J M Johnston and Mr H V de Lorey as secretaries

INFECTIOUS DISEASE IN ENGLAND AND WALES

WEEK ENDED SEPT 22

Notifications —The following cases of infectious disease were notified during the week: smallpox, 0, scarlet fever, 1361; whooping-cough, 1093, diphtheria, 496, paratyphoid, 8, typhoid, 11, measles (excluding rubella), 397; pneumonia (primary or influenzal), 347, puerperal pyrexia, 157; cerebrospinal fever, 39; poliomyelitis, 45, polio-encephalitis, 5, encephalitis lethargica, 2, dysentery, 270, ophthalmia neonatorum, 81. No case of cholera or typhus was notified during the week.

The number of service and civilian sick in the Infectious Hospitals of the London County Council on Sept 19 was 1036. During the previous week the following cases were admitted scarlet fever, 69, diphtheria, 29, measles, 18 whooping cough, 24

Deaths —In 126 great towns there were no deaths from enteric fever, 2 (0) from measles, 1 (0) from scarlet fever, 6 (5) from whooping-cough, 5 (1) from diphtheria, 71 (9) from diarrhœa and enteritis under two years, and 4 (1) from influenza The figures in parentheses are those for London itself

Liverpool and Manchester each reported 9 deaths from diarrhœa and enteritis

The number of stillbirths notified during the week was 189 (corresponding to a rate of 28 per thousand total births), including 23 in London

THE Minister of Supply has revoked the Control of Pyrethrum (Nos. 1 and 2) Orders, which prohibited the acquisition, disposal, and consumption of pyrethrum except under licence. The Ministry hold stocks of pyrethrum flowers, which were acquired for war purposes and are now available for civilian use

In England Now

A Running Commentary by Peripatetic Correspondents

I DO not think harsh measures will have the desired effect on the Germans They themselves are harsh enough already, owing, as one German doctor said to me of his heel-click and bow, to their having been too long in the army These bowings and scrapings have become a conditioned reflex, as have also the shout and raucous voice with which they give instructions to a nurse; or snap out an order to a patient or his visitor I am trying to cure a surgeon of these things I moderate my own voice till it can hardly be heard I assume a hyperacusis till he roars him gently as any sucking dove I have introduced the psychological principles of the Oxford School of Local Anæsthesia to keep him quiet and I hope that soon he will roar him an 'twere any nightingale

Then there is the civilisation of the kitchen They have no kettles, only "*kessels*," which we should call cauldrons or pots. How then can they make tea when they cannot take the pot to the kettle? In this they may have developed in the wrong direction, for I have seen kettles, good brass ones, in the Volksmuseum of the little near-by town They have, however no idea of warming the pot, nor indeed of serving food on hot plates. All these things we need to teach them Not that we should try to make them take to all our English ways If for instance, they prefer to sleep under these huge bundles, so inimitably described by Mark Twain in his *Tramp Abroad* we should not try to compel them to take to sheets and blankets in an era of world shortage of both these articles Presumably some do wake up in the morning with the thing still over them, though none of us can ever do so, and we have to admit there have been times when our sheets and blankets were on the floor and we left cold without them Yes! I am all for mild measures such as these, rather than fierce ones emulating their recent ways.

* * *

Whatever else Mussolini did, he built the Italian nation fine hospitals The one we were stationed near though bomb chipped, was modern and well equipped At our first visit our greatest difficulty was in distinguishing the medical staff from the male attendants Custom and the razor-blade shortage had combined to cover all in a three-day stubble, and all wore white coats After discussing gastrectomies for half an hour with a perplexed and inarticulate floor-sweeper, or asking the doctor sharply for our hats, we finally discovered the technique of opening a conversation with a raised eyebrow and a questioning "Professore?" They either shook your hand enthusiastically or found you one

Our guide, a young intelligent doctor, invited us to see the professor at work The theatre was equipped with every type of auxiliary apparatus and tiled in pastel shades Students peering down through the plexiglass roof could see the professor commencing the fifth gastrectomy of the morning In accordance with the Continental anæsthetic routine, the patient, after Omnopon' and scopolamine, received a somewhat perfunctory abdominal infiltration of local anæsthetic She complained stridently, releasing a quick burst of 'mammamia's" At a nod from the surgeon a mask was clapped over her face and ether lavishly poured on The anæsthetist was a little raw and nervous but succeeded finally in stilling the yells Being in doubt as to the depth of the patient he called over a colleague 'un assistente,' who without more ado, retracted the woman's lids, took out his cigarette lighter, and struck it—presumably to test the pupillary reaction The quick explosive flash and the stimulation of the burning mask proved the patient to be adequately deep

The spirit of incendiarism was even more rife at our next visit Open ether was again given and the patient was soon smoothly relaxed but the professor, feeling a little chilly that morning, instructed a nun to switch on the electric fire in the far corner of the theatre A few minutes elapsed before the slow sweeping waves of ether reached the hot wire This time the explosion was tremendous and altogether too much for the staff who took to their heels and fled, leaving the patient quietly burning on the table It says much for the battle training of our anæsthetist that, crawling from his hiding, he controlled the spreading flames Nobody was hurt and the patient didn't turn a hair

This martial experience cemented our friendship with the younger assistentes and we had the opportunity of studying the inner mechanisms of a modern Italian teaching hospital On the positive side we found the staff much more widely read and erudite than their English counterparts. They knew intimately a great deal of German, French, and American medical literature British medicine doesn't rank very highly with them: one in fact said, 'Penicillin is the only discovery that you have made since Harvey's time" Technically they were slick but too inclined to perform an operation for its mechanical beauty rather than the patient's good The number of gastrectomies all superbly done, following a history of a few months dyspepsia and a doubtful X ray finding, was incredible There was, of course, no follow up system

The nursing in the hands of the nuns, was deplorable, the ward dressings, done by a surgeon smoking a cigarette, were pre-Listerian. Local anæsthesia was roughly and hurriedly achieved, and open ether was the only substitute except a German machine that nobody could work Since they have no degree comparable to FRCS, Italians depend for their surgical maturation on the production of innumerable papers Our guide of the first day, though only 27, had 25 papers to his credit These are too often merely chunks of bibliography with trivial original material Perhaps it is all a matter of national temperament As our cheerful and prolific guide said, "We are so much more romantical"

* * *

Just before the end of the Italian campaign one of our surgical colleagues came back in great excitement after foraging among some captured German material He had found a box of yellow powder, perhaps 5 lb in all, which was described by the German label as a powerful anti bacterial substance for local wound application Being of a volatile nature he cried, "At last, German penicillin! I knew they had some And what efficiency—they are even issuing it to the individual soldiers!" It was with some difficulty that he was persuaded to have a bacteriological and chemical check, so inspired was his certainty It came back sulphonamide powder and proflavine

* * *

This is a land where the tempo of life is and always has been leisurely, for it is deep in the South, where folk have always enjoyed their living and taken their time over it, noticing and appreciating the simple things, to the envy of their harassed brothers and sisters of Chicago, New York, and the industrial North East The very names of the region—Louisiana, Mississippi, and Arkansas—conjure up the humour of Mark Twain, while the nearby city of New Orleans spreads its ancient French and Spanish influence all around This is the city famed for its Creole food and for its Mardi Gras festival as old as that still held in the little Belgian village of Binche near Mons.

Typical of these people was an old friend of mine, of 70, who still has a huge dental practice After fifty years of dentistry his skill and industry are such that he rises at 5 AM and often works until 9 in the evening, making all his dentures with his own hands He has long since ceased to concern himself with book keeping—receipts are scrawled on any available slip of paper in pencil, with a hand that shakes though it is sure and painless when using the drill He has a sense of humour very like that of the late Will Rogers whom he also resembles in appearance, and in his simplicity and directness

The eve of my return North, a large family picnic was arranged, and, boy like, he insisted on choosing and buying a water melon I accompanied him on this important mission and was delighted with his little homily on this particular fruit Young man" he said, "when you choose a water-melon, be sure and pick the biggest one you can find Unlike most things the bigger they are the better they are" And to be sure, after searching for several minutes in the ice-water tank, and spurning the assistance of the small boy in charge, he lifted out what was undoubtedly the father of all water melons It weighed exactly 50 lb He was perfectly right Even the rest of the family, always reluctant to give credit among their own members, agreed that it was delicious

Letters to the Editor

TOO MANY MEDICAL JOURNALS

SIR,—On Sept 22 you remarked (p 388) that the new *Proceedings of the Association of Clinical Pathologists* "will be welcome to many besides the group who have founded it" It will also be unwelcome to many others, or at least received with mixed feelings!

On p 383 of the same number two correspondents complain that the authors of a recent publication were unfamiliar with papers and advertisements which appeared in the *Journal of the Medical Association of Eire* While it is today very difficult for authors not to overlook something already published, the modern tendency to facilitate publication by increasing the number of specialist journals complicates matters still further

Reorganisation of all medical and scientific journals on a national, or *preferably* an international, basis is long overdue Early dissemination of the fruits of research is laudable, but the multiplicity of journals of different page size and layout—and possibly publishing highly specialised material which should appear elsewhere—is altogether bad Of the 130 different publications in English which we take at the Wellcome Physiological Research Laboratories I have to make myself familiar with the contents of at least one-third. This results in my having to "read" 650 separate numbers during the course of a year Perusal of the literature of any subject should neither take as long as it does, nor involve a risk of missing important articles Moreover, methods of filing should be capable of simplification by more collaboration and planning, and less rivalry, on the part of editors and publishers. Prompt action is necessary, for the situation is likely to worsen as supplies of paper become more plentiful There is a widespread and growing feeling that a conference should be called at which representatives of learned societies would discuss the whole problem of scientific publication, including the preparation and circulation of abstracts

Beckenham H J PARISH.

CURARE IN ANÆSTHESIA

SIR,—Professor Macintosh in his letter of July 28 utters a word of warning re the dosage of tubocurarine chloride (BW Co) While I would support his statement that the dosage required is considerably less than that of 'Intocostrin,' it is necessary to give a further caution The dose which he says he has never had to exceed for upper abdominal operations—70 mg—seems excessive In a series of over 100 cases it has never been necessary to use more than 30–35 mg for upper laparotomies, and the average dose for lower abdominal cases has been 20 mg Even in cases requiring complete paralysis of the diaphragm—e g, lobectomies, diaphragmatic hernia, &c—a dose of 40 mg has been adequate I must add that in all these cases the supplementary anæsthesia has been in the lightest plane Further confirmation of this range of dosage has been received from Dr Halton in a personal communication covering a series of such cases

T CECIL GRAY.

Department of Anæsthesia, University of Liverpool

SINGAPORE

SIR,—Singapore has fallen and the aftermath of war must now be fought The Japanese (or Nipponese as we call them in the Far East) did literally nothing for Allied prisoners-of-war, internees, and the local population I spent a week in Singapore while serving in HMS *Sussex*, so my information is first-hand By the time this letter is published the majority of Allied prisoners and internees will have left, but the local civilians remain and are being looked after by former internees who have volunteered to remain The chief of these is the Anglican Bishop of Singapore, and he has arranged for the distribution of any medical supplies that may be sent Malaria, dysenteries, beriberi, pellagra, and other deficiency diseases are but a few of the many diseases present As an illustration of how rampant some of them are, there is among the local population 80% chronic malaria and 1000 fresh cases per month Many need urgent attention which only the necessary medical supplies can ensure

Many are the humane calls made upon the good in heart, but may I appeal to institutions and individuals for any drugs they can spare—especially those used in the treatment of the diseases mentioned above? Please send them direct to the Bishop of Singapore, the Cathedral House, Singapore IAIN M. MACLEAN

FACULTY OF OPHTHALMOLOGISTS

SIR,—Meetings between representatives of the council of the Faculty, the council of the Association of British Ophthalmologists, and the council of the Ophthalmic Group Committee (British Medical Association) have been held Agreement has been reached regarding the constitution of the Faculty, including new criteria for membership and associateship, and revised arrangements for the election of council For the original statement on the formation of the Faculty, reference may be made to your issue of Feb 3, 1945 (p 156)

As a result of this agreement the council of the Association of British Ophthalmologists were enabled to urge all their members to join the Faculty and to approve the dissolution of the Association in order that it may be merged into the Faculty A postal ballot of members of the Association has revealed the necessary majority in favour of dissolution A new council of the Faculty is to be elected after due time has been allowed for all, including serving ophthalmologists, to join the Faculty, in the meantime any applications for membership or associateship which present any doubt are to be scrutinised by a joint committee representing the council of the Association of British Ophthalmologists and the present council of the faculty

The following are the new criteria

MEMBERSHIP

1 Any ophthalmologist of the status of ophthalmic surgeon or assistant ophthalmic surgeon, who holds an appointment on the staff of a voluntary or municipal hospital with a recognised eye department
2 Any ophthalmologist, no longer on the active staff of a hospital, who has held such an appointment.
3 Other ophthalmologists of consultant rank approved by the council, including those in the Services or holding Government appointments, and those of the British Commonwealth and Empire overseas

ASSOCIATESHIP

1 Full-time ophthalmologists of two years' standing
2 Part-time ophthalmologists of two years' standing, holding a hospital appointment or possessing a special diploma
3 Practitioners who on June 1, 1945, were on the list of the National Ophthalmic Treatment Board

COUNCIL

The council shall be increased in number to 25, the number of regions to be increased to 6, to correspond with the regions defined by the British Medical Association

The council shall be constituted as follows (*a*) One member shall be elected from each region by a local regional vote of members (*b*) Twelve members shall be elected by a national vote of members (*c*) One associate shall be elected from each region by a local regional vote of full-time associates, representing the full-time associates. (*d*) One part-time associate shall be elected by a national vote of part-time associates, representing part-time associates (*e*) Any member of council shall be free to stand for election indefinitely, if properly proposed and seconded

The outline of the constitution, functions, and management of the Faculty included in the statement which you summarised in February, amended as above, will in general terms remain valid As soon as the new council is elected, the constitution and by-laws will be legally drawn up Forms of application for membership or associateship of the Faculty may be obtained from the hon secretary, 45, Lincoln's Inn Fields, London, WC2

STEWART DUKE-ELDER, President
FRANK W. LAW, Secretary
Faculty of Ophthalmologists

J N TENNENT, President
H. R BICKERTON, Secretary
Association of British Ophthalmologists

THE "PERFECT AP"

SIR,—When, in 1935 at Oxford, Jacobeus reported to the Tuberculosis Association that his experiments in differential bronchospirometry showed the lower lung in lateral decubitus) to be performing more work than the upper lung, it came as a great shock to us all It seemed so unreasonable Jacobeus agreed that it was unexpected, unreasonable, and disturbing, and was almost apologetic about it It occurred neither to him or to anyone else that his observations were invalidated because his subjects had lain in an "unnatural position" as suggested by Dr Fraenkel in your issue of Sept 15 Some other explanation seemed necessary

Some time later I tried some crude experiments in differential cytometry (using an ordinary tape measure): I measured the expansion of each hemithorax with the subject standing, lying on the left side and lying on the right side, and there appeared to be nothing in it obviously therefore (although I didn't see it for another couple of years), if indeed more air passed in and out of the "under" lung, it could only be due to an increased excursion of the "under" hemidiaphragm Dr Wynne Edwards and I next rigged up a couch behind the X ray screen, so that subjects could be viewed lying on either side We discovered that

(1) The "under" hemidiaphragm had a greater excursion In full inspiration it was about level with the upper one but in full expiration it bulged much further into the thoracic cage

It seems reasonable to suppose that this was due to the greater weight of loose abdominal viscera pressing on it, but we also found that

(2) The heart and mediastinum sagged into the lower lung in full expiration, whereas in full inspiration they lay pretty well in the midline behind the sternum

In fact, the zone of the "under" lung thus boxed in by sagging mediastinum and apex ward thrust hemidiaphragm became radiologically quite dense, which we took to mean that we were viewing concentrated lung tissue with very little residual air in it In full inspiration the translucency was normal.

Maybe we were wrong in our observations and inferences Maybe we also chanced to get our subjects into "unnatural positions." If so it would be a good thing to discover how to achieve these unnatural positions, and to get those patients who prefer to sleep on the unaffected lung to adopt them

Birmingham GEORGE DAY

DEAD HAND

SIR,—It is possible that Telford, McCann, and MacCormack in their article of Sept 22 had in mind the use of the flexible shaft equipment now so common in industry If this was the tool concerned, then I also have seen Raynaud's syndrome in users of this tool and this fact was noted in the *British Journal of Industrial Medicine* last year (1944, 1, 179) The flexible shaft equipment is a very large dentist's drill driven by an electric motor developing quite large horsepower for so small a concern Using this tool one of the workers was noted to have developed symptoms of dead fingers in under a year He was unskilled and being on piece work used the motor at top speed (7000 r p m) This applied to two other sufferers I saw at that time

The mechanical details of this tool have a bearing on the medical problem As in a dentist's drill various end-attachments—mops, soft polishing wheels emery or composition wheels and burrs—can be fitted and all of these are in various sizes The attachment in use influences the amount of vibration The electric motor in the type I saw can be run at three speeds and the highest speed much increased the vibration It seemed also that the larger the diameter of the end-attachment the more severe was the vibration Other important factors were the length of spindle connecting end-attachment to tool efficient greasing of the internal parts of the flexible shaft adjustment of the bearings in the hand pieces, and avoidance of kinking in the shaft during use The more the shaft was curved, the more vibration resulted Unskilled workers got more 'bump' than necessary and increased the jarring effect Also the foreman was certain that too much pressure was often used by the unskilled employee A long spindle was often quite unnecessary and greatly increased vibration although for a few jobs this length is necessary

It is possible that attention to these points might lessen the harmful effect It is also possible that there is a harmful vibratory range as Hunter, McLaughlin and Perry recently pointed out (*Brit J indust Med* 1945 2, 10), when discussing pneumatic tools There may be harmless vibratory levels above or below (or both) the harmful vibratory range

Oxford G WHITWELL

MEDICAL FILMS

SIR,—On rounds and in outpatients, cases are presented and seen—by those who have a front seat—and discussed, and treatment is detailed But generally the student never sees the result of treatment A short teaching film, preferably with a succinct precise commentary, could present the diagnosis treatment, and results How much more vividly would the memory retain such a satisfying sequence

Middlesex Hospital. R N S ATHERSTONE.

VITAMIN-B DFFICIENCY AND NERVOUS DISEASE

SIR,—Dr Walshe in his interesting letter of Sept 22, discusses the general inference that can be drawn from your leader of Sept 8 In his experience the clinical course of polyneuritis has not been materially altered by the introduction of vitamin B therapy

I have no experience of the treatment of this affection in the pre vitamin era, but during the past few years I have treated or supervised the treatment of some two hundred cases of polyneuritis, excluding those of obviously infective origin The majority of cases were seen in malnourished people in the Middle East—Polish refugees Arab, African, and Indian natives, and German and Italian prisoners-of war In this country I have recently followed the course of the affection in many malnourished German troops from the Channel Isles and in chronic beriberi patients from POW camps in the Far East Apart from relief of pain and tenderness in some acute cases I cannot say that thiamine or the whole B complex, in large doses and by all routes, exerted any apparently beneficial effect Rest in bed and good food were equally effective In the vitamin treated cases the restoration of power sensibility, and reflex activity was not hastened The patients were just as long in bed and just as long in hospital I concluded that if vitamin B_1 is the "antineuritic" vitamin the results of therapy in chronic polyneuritis cannot be quoted in support of that contention, despite any properties B_1 may possess in combating the acute beriberi of the Far East

My experience thus confirms that of Brown (1941) although her data were not based on personal experience Ability to walk was the main criterion for discharge from hospital, but during the period covered by her paper (1920–38) there may not have been complete uniformity of view on this question among the many interns concerned All the cases were of the alcoholic form of polyneuritis, and it is interesting to recall that from the same hospital in Boston emanated one of the earliest reports suggesting the vitamin B deficiency origin of alcoholic polyneuritis (Minot et al 1934)

What of the experimental evidence?

It was a strange fate that provided Eijkman with pigeons for his experiments in the Java jail, for subsequent studies have shown that the pigeon is an animal in which deficiency paralysis can easily be induced In other animals dogs for example the susceptibility is much less Some workers have quite failed to induce significant polyneuritis by feeding animals on diets deficient only in thiamine (Kon and Drummond 1927, Moore et al 1932, Grinker and Kandel 1933 and Prickett 1934) while others have found that starvation is no less effective (Chamberlain et al 1941 Woollard 1927, Davison and Stone 1937, Vedder and China 1938) In man experimental deficiency of thiamine is reputed to produce signs of "neurasthenia"—such as headache loss of appetite lack of energy irritability and inefficiency—and is sometimes accompanied by symptoms and signs of mild neuritis of the feet and legs (Williams et al 1939 1940 1941 1942 Jolliffe et al 1939, Thom et al 1935, 1940, O'Shea et al 1942) But in one of these

series (Williams et al 1940) five of the experimental subjects were formerly psychotic! This body of evidence is therefore not conclusive although recently Swank and his colleagues (Swank et al 1941, 1942, Prados et al 1942) have satisfied themselves that deficiency of thiamine alone may produce polyneuritis in experimental animals

When Walshe (1918) described beriberi in British soldiers in Alexandria he stressed the significance of the high content (500 g) of carbohydrate in their Mesopotamian rations, and his suggestion of aberrant carbohydrate metabolism was confirmed experimentally by Peters and his associates (1936) They showed that in the presence of carbohydrates thiamine deficiency led to the accumulation of an intermediate metabolite—pyruvic acid—and Platt and Lu (1936) repeated this observation in human beriberi From the ætiological point of view we are thus back where we were when Eijkman postulated that foods such as polished rice, being over-rich in carbohydrates, produced a substance in the intestine which was poisonous to nerve-cells and for which the outer layers of the rice grain acted as an antidote This theory is of interest in the light of the recent demonstrations that vitamins are synthesised and destroyed in the bowel of man by microflora—and possibly by other agencies

With regard to the syndrome Scott and I described, your leader stated that "the evidence suggests that this neuropathy was a manifestation of riboflavine deficiency" As we explained, only a few of our patients had had symptoms of ariboflavinosis, and treatment with the entire B complex and with riboflavine, even early in the disease, gave quite inconclusive results It is true that riboflavine deficiency in the dog can produce certain neurological disturbances—collapse and coma in complete deficiency, and ataxia and paralysis in chronic partial deficiency But loss of sight and deafness, which were prominent in our series, have not been recorded in riboflavine deficiency On the other hand they have been described in experimental B_1 deficiency (Peters 1934, Selfridge 1939) In man the mucocutaneous lesions of riboflavine deficiency, though they sometimes coexist with beriberi or pellagra, may persist or recur for several years without the appearance of neurological signs. No neurological symptoms developed in the women rendered deficient of riboflavine by Sebrell and Butler (1938) We are thus in no position to relate the neurological syndrome described to deficiency of riboflavine and it would be unwise to speculate at this juncture A repetition of the premature incrimination of vitamins E and B_6 (pyridoxine) in the ætiology of motor neurone disease, the muscular dystrophies, and paralysis agitans, would be unfortunate

The current misuse of vitamin B in clinical medicine is such that an authoritative statement concerning its value and limitations is most desirable

York J W SPILLANE

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Obituary

WILLIAM THOMAS

M B, B SC LOND

THE death of Dr. William Thomas will be widely felt in the Clapham district, where he had laboured for most of his professional life One of three brothers who received their medical education at St. Thomas's Hospital, he early gave evidence of ability by taking his B Sc with first-class honours in chemistry within a few days of his 19th birthday, and publishing a paper (jointly) in the *Transactions* of the Chemical Society on the colour and constitution of the azo-compounds. At St Thomas's he was awarded the senior entrance scholarship in natural science in 1911, and the William Tite scholarship in the succeeding year. He became in turn demonstrator of biology, chemistry, and toxicology, and while studying medicine he found time to write articles on such subjects as diseases of trout, and the pollution of streams, which had excited his curiosity

Qualifying as MRCS in 1915, he held the posts of casualty officer and resident anæsthetist at St Thomas's, and then joined the RAMC, in which he served as a battalion medical officer in France and Salonika, being mentioned in despatches He married during the war, and on returning took his London MB Many of his friends thought that this quiet, reserved, and studious man was destined for a life of research in a laboratory, but his choice of a career was to settle down to general practice within a stone's throw of his old home.

In Clapham he held several appointments and for 25 years was a popular divisional surgeon to the Metropolitan Police. Although he had no mean artistic and musical ability, he preferred to devote all his time, as he put it, "to overwork and oversmoking" He proved himself a skilful physician, with a fine disregard of the monetary rewards of his profession He was only 57 years of age when he died, but "he husbands best his life that freely gives it for the public good"

Appointments

*WOLMAN, BASIL, MB MANC, MRCP temp deputy medical superintendent, Withington Hospital, Manchester
*KIRKMAN, N F, MD MANC, FRCS temp RSO, Withington Hospital, Manchester
PILLAI, SUNDRAM, MB, DOMS, DLO RSO, Hull Royal Infirmary
BARRON SAMUEL, MRCPI, DPH medical superintendent officer of health and port MO for Belfast
SPIRO, ISIDORE, FRCS temp. ophthalmic surgeon, Queen Mary's Hospital for the East End, London

* Subject to confirmation

Births, Marriages, and Deaths

BIRTHS

BAIRD —On Sept 21, at Southborough, the wife of Captain J T Baird, RAMC—a son
BENNETT JONES —On Sept 25, the wife of Mr M J Bennett-Jones, FRCS, of Gateacre, Liverpool—a son
DUFFIELD —On Sept 19, the wife of Dr John Duffield, of Littlemore, Oxford—a daughter
HORSFALL.—On Sept 21, in London, the wife of Surgeon Lieutenant W R Horsfall, RNVR—a daughter
MACIVER —On Sept 27, at Newcastle on-Tyne, the wife of Captain Ian Maciver RAMC—a daughter
MCOWAN —On Sept 23, the wife of Surgeon Lieut -Commander B M McOwan, RNVR—a daughter
MAGEE.—On Sept 23, in London, the wife of Dr C Gaulter Magee—a daughter
O'NEILL —On Sept 19, at Barnet, the wife of Surgeon Lieutenant Barry O'Neill, RNVR—a daughter
PERCIVAL —On Sept 25, in London, the wife of Surgeon Lieut-Commander R. O Percival, RNVR—a daughter
WATT —On Sept 24, at Aberdeen, the wife of Dr Leslie Watt—a son

MARRIAGES

BARBOUR—BOUQUET —On Sept 22, in New Delhi, G B Barbour MB, squadron leader, of Dulwich, to J A Bouquet, section-officer, of Sydney, Australia

DEATHS

BOWDLER.—On Sept. 26, at Bournemouth, Archibald Penrhyn Bowdler, OBE, MA, MB CAMB, formerly of Chiswick
DE MOWBRAY.—On Sept 24, Ralph Marsh de Mowbray, FRCS, of Lymington, Hants
HAMILTON —On Sept 24, Alexander Keith Hamilton, MB LOND, formerly of Tiverton, Devon
MCDOUGALL.—On Sept 29, at Wallington, William Stewart McDougall, MB EDIN
TRAVERS SMITH —On Sept 28, in London, Richard Travers Smith, MD DUBL., FRCPI, aged 73
WARD —On Sept 21, Ernest Ward, MA, MD CAMB., FRCS, of Paignton, aged 68

Notes and News

BRAZILIAN PLASTIC SURGERY

A TALK on plastic surgery in Rio de Janeiro was given in London, under the auspices of the British Council on Sept. 25, by Dr. Davis Adler, of the University of Rio de Janeiro. He showed a number of simple films, some in colour, demonstrating his technique. These included plastic reconstitution of the depressed nasal bridge by the orthodox technique for all cases of which he now uses cartilage obtained from cadavers, and stored in the refrigerator, thus avoiding two operations on one patient. For most other cartilage-insertion work, including depressed frontal bone, he prefers to use cartilage-chips rather than pre-fashioned insertions, for he finds this technique gives a more satisfactory end result. Sir Harold Gillies, on behalf of the large audience, thanked him for an instructive talk.

MIDDLESEX HOSPITAL DINNER

Lieut.-Colonel J. J. Astor, chairman of the hospital, presided at the annual dinner held at the Savoy on Sept. 28. He expressed thankfulness that the hospital had survived the war with so few casualties and so little material damage. True the annexe had been destroyed, but it was never convenient. The arrangements so carefully worked out before the war started had needed alteration only in detail. In the 200 years since its foundation the hospital had developed very high traditions and standards of service, and no effort would be spared to maintain them. Dr. H. E. A. BOLDERO, dean of the medical school, recalled that the previous annual dinner was held on the day Mr. Chamberlain returned from Munich. After the war began the preclinical students went to Bristol for three months; in 1940 they went to Leeds where they had two happy years under the care of Prof. J. Kirk, the sub-dean, and in 1942 they came back to London which he hoped they need never again leave. Clinical students had been distributed between the Middlesex Hospital itself, the Central Middlesex Hospital, Mount Vernon Hospital and Tindal House, Aylesbury, and some had not yet returned. The past few years had brought many honours to Middlesex men—among them Prof. E. C. Dodds, FRS, Sir Alfred Webb-Johnson, FRCS, and Sir Lionel Whitby, regius professor of physic. In the Services they mostly seemed to attain consulting rank, and among those present he was glad to see Brigadiers McAlpine, Bedford, and Marriott. At home Prof. B. W. Windeyer had made a real success of his war-time office of hospital commandant: "quiet or noisy day or night he was always the same to every body, and what better could you say of an administrator?" Despite diversions such as D-day and Belsen, students had qualified in good time; and Dr. A. S. Burgen this year's Broderip scholar, had won the university gold medal with distinction in five subjects. The task now before the hospital was to put the jigsaw pieces back into a pattern even better than before. Eleven places on the medical and surgical staff had to be filled, and they should be filled without haste. Dr. BURGEN, who said he had enjoyed his travels departed from tradition by reporting no complaints. Sir ALFRED WEBB-JOHNSON, proposing the health of the Chairman, spoke of his recognition that the staff should be partners with the board in running the hospital. He hoped the future would include plans by which the staff could carry on private consultations with the background of the hospital behind them.

Diploma in Industrial Health

The Society of Apothecaries of London has instituted a diploma in industrial health, which will be open to registered medical practitioners who have been engaged in whole-time practice of industrial medicine for not less than two years, or in part-time practice for not less than four years. The society understands that courses in the subject are to be held in the future, and these subject to their fulfilling the requirements laid down in the society's regulations will be recognised as qualifying for admission to the examination for the diploma. The syllabus and regulations covering the examination will shortly be obtainable from the registrar of the society, Black Friars Lane, Queen Victoria Street, London, E.C.4.

University of Sheffield

At recent examinations the following were successful:

FINAL EXAMINATION FOR MB, CHB

Parts II and III—Jack Edwards (second-class honours), Aileen K. Adams, Harry Debovitch, Colin Gething, A. I. Hayhurst, Ronald Horn, J. K. Heilson, O. M. King, John Mackinnon, J. B. Mansfield, Cora H. M. Middleton, Monica H. Roper, Margaret M. Swyan, Joan Simson.

University of London

Mr. J. Z. Young, FRS, has been appointed to the university chair of anatomy at University College. He is a fellow of Magdalen College, Oxford and university demonstrator in zoology. Since 1940 he has been a member of the Nerve Injuries Committee of the Medical Research Council.

Prof. F. G. Young, D.SC. has been appointed to the University chair of biochemistry at University College. Since 1942 he has held the chair of biochemistry at St. Thomas's Hospital.

University of Leeds

Mr. Raymond Priestley, D.SC., principal and vice-chancellor of the University of Birmingham, will deliver the inaugural lecture of the faculty of medicine on Monday, Oct. 15, at 3 P.M. His subject is to be Scott's Northern Party—a study of survival in the Antarctic.

On conferring medical degrees recently the Vice-Chancellor (Mr. B. Mount Jones) said that 990 applications had been received for admission to the medical school for the new session to fill 75 vacancies. Already the number of applications for the following session was well above the places available. Even when building permits were eventually received to extend their present accommodation so as to deal with an annual intake of 100—the maximum considered desirable—it would still be impossible, said the Vice-Chancellor, to satisfy the demands for admission if they maintained their present rate. It was well that this should be known so that parents could contemplate alternative careers for their sons and daughters.

University of Aberdeen

On Sept. 26 the following degrees were conferred:

MD—A. D. Forgie.

CAM—**G. O. Lennon, *J. L. Stephen.

** With honours. With commendation.

MB, CHB—Marjorie J. G. Allan, Barbara E. Anderson, Janet W. Anderson, James Barr, H. S. Bennett, Vera G. A. Booth, R. J. Bruce, Joan M. Burrell, J. S. Caldwell, Jane E. Cambell, J. A. Chalmers, J. D. Chalmers, Frances R. Christie, W. G. C. Craigen, D. S. Cramond, R. S. Crow, R. P. Cumming, J. D. Davidson, L. K. Dawson, J. U. Dods, F. F. Ducat, J. G. Duncan, Donald Beattie-Smith, A. G. C. Findlater, J. A. Gavin, Margaret W. Gibb, Gladys M. Gill, Eva C. G. Gray, Mary F. Gray, H. S. Heddle, W. M. Ironside, Mary K. Johnson, A. M. Knox, D. J. Lyall, K. F. McIver, Catherine H. Mackie, A. I. Macleod, J. R. McPherson, Gertrude M. Mennie, Thomas Menzies, Catherine H. Mitchell, G. W. Morrison, Kathleen M. Morrison, S. S. S. Munro, Kathleen M. I. Murray, J. M. Park, Doris Ramsay, J. C. Reid, J. S. Ritchie, William Ritchie, Griselda M. Seggie, J. G. Shirreffs, Agnes M. Sleigh, Evelyn A. Souter, G. P. Sutherland, C. M. Taylor, Jean C. Taylor, W. C. Taylor, Mary A. Templeton, James Watt, Violet I. Wilson.

University of Liverpool

Mr. C. A. Wells has been appointed to the chair of surgery in succession to Prof. O. H. Williams, and Dr. T. N. A. Jeffcoate to the chair of obstetrics and gynæcology in succession to Prof. A. Leyland Robinson. Hitherto professors of clinical subjects have continued in private practice, but to meet the growing responsibilities falling upon the medical school it has been decided to make these new appointments whole-time. Beds will be at the disposal of the new professor of obstetrics and gynæcology at the Liverpool Maternity and Women's Hospitals and it is expected that the professor of surgery will have beds at the Royal Liverpool United Hospital.

Mr. Wells, who is 47, graduated MB with honours at the University of Liverpool in 1921 and after holding a resident appointment at Ancoats Hospital, Manchester, he became lecturer in anatomy at Mcgill University. He returned to England as surgical registrar and senior surgical tutor at the Royal Infirmary, Liverpool, where he settled in practice as a surgeon. He is at present surgeon to the Liverpool Royal United Hospital, consultant to the Women's Hospital, the Maternity Hospital, the Cheshire county council and in urology to the Lancashire county council. He also lectures on the practice of surgery at the university. His *Manual of Surgery for Nurses* appeared in 1938, and he has described an operation for high gastric ulcer and also written on tuberculous epididymitis.

Dr. Jeffcoate, who is 39, is at present gynæcological tutor in the university. He took his MB Lpool with first-class honours in 1928 and obtained his MD three years later. A fellow of the Royal College of Surgeons of Edinburgh and of the Royal College of Obstetricians and Gynæcologists, he is on the staff of the Liverpool Maternity Hospital, the Women's Hospital and the Daryl Lewis Northern Hospital. He was responsible for setting up new departments of midwifery and gynæcology in the Royal Infirmary, Wigan, and the Hitchcock Maternity Hospital, Wallasey. He has published papers on ovarian dysfunction and for his Hunterian lecture in 1938 chose the subject of uterine inertia.

Institute of Laryngology and Otology

A five-weeks' course of lectures and demonstration in laryngology, rhinology and otology for postgraduate students—especially those taking part II of the DLO examination—will be held at the institute, 330 Gray's Inn Road, London, W.C.1, from Oct. 29 to Nov. 30.

Royal College of Physicians of London

On Thursday, Nov 8, at 5 PM, Dr W Russell Brain will deliver the Bradshaw lecture at the college, Pall Mall East, SW1 He is to speak on Speech and Handedness

Radcliffe Infirmary, Oxford

Dr Janet Vaughan, principal of Somerville College, has been appointed consulting hæmatologist to the infirmary

British Dental Association

Mrs Lilian Lindsay, LDS, has been appointed president-elect of the association

Ex-Services Welfare Society

This society is holding a medical conference at the Royal College of Physicians of Edinburgh on Friday, Oct. 5 Prof D K Henderson will take the chair at 10 30 AM.

Advisory Committee on Welfare of the Blind

The Minister of Health has appointed Lord Rushcliffe to be chairman of this committee in succession to Lord Blanesburgh who has resigned

Eugenics Society

On Tuesday, Oct 16, at 5 30 PM, at the rooms of the Royal Society, Burlington House, Piccadilly, London, W1, Dr W Mayer-Gross will speak on mental health problems in a rural area

Medical Women's Federation

The annual general meeting of the federation will be held today, Friday, Oct 5, at the Imperial Hotel, Temple Street, Birmingham, at 7 30 PM. Afterwards Dr Helen Mackay will speak on the Health Centre and a Child Health Service.

Nursing Education

The Liverpool Staffs Association, consisting of the honorary medical staffs of the nine Liverpool teaching hospitals, has recently passed the following resolution

This association express their deep concern with the increasing trend towards demanding of nurses too detailed a theoretical and scientific knowledge, to the discouragement of practical craftsmanship The members of this association believe that the qualifying standard for registration should be based very largely on practical experience and vocational training For all higher and specialised forms of nursing, a further and more scientific type of training should be demanded

Royal Society of Medicine

On Tuesday, Oct 9, at 5 PM, Sir Percival Hartley, D SC, FRS, will deliver the Dixon lecture to the section of experimental medicine and therapeutics He is to speak on international biological standards On the same day, at 5 30 PM, Dr G W B James will give his presidential address to the section of psychiatry on psychiatric lessons from active service On Oct 10, at the section of comparative medicine at 2 15 PM, Mr W A. Pool, MRCVS, as his presidential address, will make a plea for the eradication of tuberculosis in cattle in Great Britain, and afterwards Prof. Thomas Dalling, MRCVS, and Mr J. N Ritchie, MRCVS, will demonstrate tuberculin and other materials used in this country and the USA in connexion with the eradication of bovine tuberculosis At 4.30 PM, at the section of physical medicine, Dr J W T. Patterson will give his presidential address on physical medicine in the Army and civilian practice At the section of ophthalmology, on Oct 11, at 5 PM, Prof Arnold Sorsby will speak on penicillin The clinical section will meet on Oct 12, at 5 PM, to hear Mr Dickson Wright's presidential address on hysteria

Wellcome Directors

Wing-Commander C J Hackett has been appointed director of the Wellcome Museum of Medical Science in succession to Dr S H Daukes who is retiring after 26 years' service Dr E Ashworth Underwood has been appointed director of the Wellcome Historical Medical Museum and Library

Dr. Hackett took his MB at the University of Adelaide in 1927 and his MD in 1935, and after holding a lectureship in physiology there he came to this country to take the DTM&H in 1930 and the MRCP the following year As senior research fellow in tropical medicine to the Medical Research Council he published papers on yaws and syphilis in Australian aborigines During the war he has held a commission in the RAFVR and he will take up his new appointment as soon as he is released from the Service

Dr Ashworth Underwood is a graduate in arts, medicine, and science of the University of Glasgow Qualifying in 1921 he was awarded his MD with high commendation in 1926 He has held appointments in the public health services of Shoreditch and Leeds, where he was also lecturer in public health at the university, and for the past eight years he has been MOH for West Ham Dr Underwood is secretary to the history of medicine section of the Royal Society of Medicine and besides his published works on epidemiology he has written on the French chemists and the earlier anatomist. He is at present collaborating with Prof Charles Singer in a work on Vesalius

Medical Society of London

On Monday, Oct 8, at 8 30 PM, at 11, Chandos Street, London, W1, Sir James Walton will deliver his presidential address on the ætiology of gall stones

Society for the Study of Inebriety

At a meeting of the society to be held on Tuesday, Oct 16, at 4 PM, at 11, Chandos Street, London, W1, Sir Adolphe Abrahams will read a paper entitled A Layman looks at Alcohol

British Council Lectures in Scandinavia

Prof E C Dodds, FRCP, FRS, is visiting Norway, Sweden, Denmark, and Finland, under the auspices of the British Council, to lecture on cancer research and biological and medical subjects.

Research Defence Society

The annual general meeting will be held at 26, Portland-Place, London, W1, on Friday, Oct 12, at 3 15 PM. Afterwards Sir William Savage will deliver the fourteenth Stephen Paget lecture, on public health and its debt to experimental medical research

Socialist Medical Association

On Friday, Oct 12, at 7 30 PM, at Friends House, Euston Road, London, NW1, Mr F Le Gros Clark, secretary of the Children's Nutrition Council, is to give an address entitled World Famine this Winter ?

Royal Medical Society of Edinburgh

Dr Charles Hill will give the inaugural address of the 209th session of the society at 8 PM on Friday, Oct. 12, on the future of medical practice The meeting will be held at 7, Melbourne Place, Edinburgh, 1. During the session addresses will also be given by Mr F G Gibbs, parodontal disease (Nov 9), Colonel Walter Elliot, medicine and the State (Nov 23), Dr Halliday Sutherland, the life and work of Sir Robert Philip (Jan. 11), Prof. Dugald Baird, population problem (Jan 25), Prof H. Dryerre, physiology of sex hormones (Feb 8), and Mr K. Paterson Brown, the unexpected in surgery (Feb 22)

Return to Practice

The Central Medical War Committee announces that the following have resumed civilian practice

Mr W BARCLAY, MC, FRCSE, 5, Murray Road, Huddersfield
Dr REX BINNING, 18, Brunswick Square, Hove, Sussex
Dr LEONARD F BROWNE, 9, Harley Street, London, W1
Mr C W GORDON BRYAN, 118, Harley Street, London, W1
Dr I G W HILL, FRCPE, 14, St John's Road, Edinburgh, 12
Mr A E PORRITT, OBE, FRCS, 3, Regent's Court, Park Road, London, SW1

General Board of Control for Scotland

Brigadier T F Rodger has been appointed a medical commissioner of the board in succession to Dr A G W Thomson who has retired

Dr Rodger graduated BSc at Glasgow University in 1927 and MB with commendation two years later In 1931 he took the DPM and he was elected MRCPE in 1939 He was an assistant physician at the Edinburgh Royal Mental Hospital and assistant in psychiatry at the Johns Hopkins Hospital, Baltimore, before he was appointed senior assistant superintendent to the Glasgow Royal Asylum. In Glasgow he also acted as assistant consultant in psychiatry to the Western Infirmary, as physician to the Lansdowne clinic for functional nervous diseases, and as assistant to the lecturer in psychiatry at the university His publications include papers on effort syndrome, night blindness, and fibrositis During the war Dr Rodger has served with the RAMC and he is at present consulting psychiatrist to the India command, with headquarters at Delhi

Medical Films

At a joint meeting of the Association for Scientific Photography and the Royal Photographic Society, held in the Hastings hall of BMA House on Sept 24, Sergeant Clissna of the US Army Pictorial Service gave a talk on Medical Cinematography in 'Kodachrome' After explaining the technical details of his mode of working, in which he stressed the need for sympathetic cooperation between surgeon and photographer, both before and during the operation, he presented a film on Foreign Bodies in the Pericardium and Heart, which showed four operations for this condition

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METHYL THIOURACIL IN THYROTOXICOSIS —Pharmaceutical Specialities (May and Baker) Ltd. can now supply 4 methyl 2 thiouracil in tablets of 50 mg, 100 mg, or 1000 mg packed in containers of 100 or 500 tablets

PROFESSOR BONHOEFFER A Correction —On April 29, 1944 we published a notice of the death of Prof Karl Bonhoeffer, the leading figure in German psychiatry before the war We are now happy to announce that the report was false Professor Bonhoeffer is alive, in Berlin, and his family in England have had letters from him

ON NOTHING IN PARTICULAR

EXTRACTS FROM THE INAUGURAL ADDRESS TO STUDENTS OF THE LONDON SCHOOL OF MEDICINE FOR WOMEN

Lord MORAN, MC, MD
PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS

I SEE that those who have spoken to you before me have begun with Florence Nightingale or someone who has been a champion of your Rights Surely that is not necessary at this time of day We have gone far since the time when old Pritchard was professor of astronomy at Oxford and was known as the Heavenly Body, being the same shape as the sun and about the same size He was prevailed upon to allow ladies to attend his lectures and he began by complaining that he had been traduced "God forbid" he said, "that I should deny the light of His truth even to the meanest of His creatures"

I shall begin by warning you against being too gregarious; in this dreadfully overcrowded island we live on the top of one another, until soon we shall all be made to one pattern Once, when we were flying across the Atlantic, one of my companions said to me, 'Do you realise we are fifteen hundred miles from anywhere?' But we are not always so lucky Even when we are not talking to each other, we sit there in tube or train behind our morning or evening papers avoiding at any cost what Arnold Bennett called 'the intolerable effort of conscious thought" We are content to live on borrowed thoughts

I cannot pretend that we teachers give you much encouragement to think for yourselves We have designed your curriculum so that you rush all day from pen to pen like sheep, and we bark at your heels like sheep-dogs marshalling their flock You have never a moment to turn over in your mind what you have heard And we have contrived an examination system which threatens to question you on any bit of this curriculum, however unimportant I hear much about the shortcomings of the examinee, and little about the frailty of the examiner, and yet how many examiners there are who set out to find what the student does not know and not what he does know An examination is but a form of criticism, and no true critic, whether of book or play or piece of music, gets marks for being a destructive critic He gains repute according to his skill in putting his finger on what is good and memorable If the examiner is out to find out what the student does not know the student will take refuge in a smattering of everything but if he felt that the examiner would search for something he knew, then he might be content to master something

Let us, however, assume that when you are qualified you have learnt to think for yourself Well then, your wits need not be long idle At this moment the Government of the day is putting a fundamental question to the nation Is the stimulus of the competitive life with its prizes to the successful, the only, or even the right, spur pressing men and women on to give of their best, or will they do equally good work in a national service? If you have taught yourself to worry things out, you will answer without prejudice The question put to you is nothing less than this What is it which brings the best out of men and women?

It would be foolish to under rate the part that the money motive plays in most people's lives, and there is *indeed nothing discreditable in making proper provision* for one's family and for old age Nevertheless, I think this part is sometimes exaggerated In science you find men and women some of the most critical of our race, working for salaries, often very modest salaries, and they are perfectly happy because they are doing the work they want to do under the best conditions What has appealed to men of science will, I believe increasingly appeal to the younger men and women in our profession We must remember too that it is only yesterday that such a life has been open to members of our calling The Royal Commission of 1913 were critical of what they called "Harley Street" They complained that we were not making substantial additions to knowledge, and they advocated by way of remedy that there should be opportunities for an academic career in Medicine So there came into being the unit system, with professors of medicine and surgery and obstetrics The Commission thought that men would welcome a career which gave them more time for reading and for research and for keeping in touch with workers in other lands, and I believe that we shall find the younger generation more sympathetic to such conditions of life than we seniors have been. They will, of course, miss something which we got out of practice, but they may have to make these sacrifices in order to obtain the best conditions for a fruitful life

Before I leave this question of how far men and women are prepared to work in a service I will draw your attention to what we have learnt in war because it may have a bearing on what we plan in peace I had written a little book and had given it to Mr Desmond MacCarthy for his opinion He was very helpful in criticism, but in giving it back to me he did say, 'I do just wonder what people will think of a book written in the midst of a great war which is so largely illustrated from another war that happened over a quarter of a century ago" Immediately, I was convinced that he was right and that nobody would read my book at all But it did not turn out that way, because that book was read by the men, or at least by some of the men, who fought in the last war and who found in its pages, brought back to life, an experience which they had not forgotten, which indeed they remembered with a certain nostalgia That brings me to this question Why do men so often look back on their war experience, with its monotony, its discomforts, and its dangers, as one of the happiest times of their life? I think the answer is that it was a man's life, a life from which men who were not men had been weeded out, and that they were doing something for a cause which could not possibly benefit themselves, except very indirectly In short, it was an experiment in altruism, though they would never use that word an experiment which has been astonishingly successful And if this happens in war why should it not happen in peace? Anyone who can find an answer to that question will have made a signal contribution to the contentment of our people.

I need scarcely counsel you not to make a god of security, not to put safety first When the spirit of adventure goes out of life it is time to draw down the blinds And don't work too hard don't become a drudge In general men given great responsibility work too hard Gandhi's weekly day of silence for thought and prayer is an example to all Englishmen who hold power Gandhi found he was 'losing mental freshness, spiritual power, and was in danger of becoming formal, mechanical and devitalised'" What I wrote with men in my mind applies particularly to women I am giving you this advice because I do not want your work to deteriorate as it will if you dull your wits with long hours of toil But remember you have only one life and ask yourself what it is that makes men and women happy I suppose it is largely a matter of temperament Apart however from the way you are made, it helps to do a *job you like and to do it well to be at peace with those* with whom you spend the day And leisure is a precious thing I would have you build some sanctuary into which you can creep when the world seems a grim place

* * *

It may be that you young people sometimes feel that the graces of life have gone and that beauty has been banished from the earth you may even feel a sense of grievance that you were matched with these drab days

There is something in this But let me reassure you a little A few days ago I was in the Italian Lakes in one of the most beautiful places in the world, and then only six hours later I was in my cottage at Harefield I left my luggage and wandered into the meadows where the Jersey cows were flicking away flies with a whisk of the tail, while a soft wind blew gently through the tree tops, and when I looked up the rooks got up with a great cawing, a black cloud against the blue sky, and in the distance I could hear the sound of a mowing machine And it came to me then at the end of my wandering that there is no place in the world which is a patch on England, and that with their tolerance, their good humour, and their fair minds the graces of an old culture, there is no people half so civilised as our own countrymen And after that great burst of brazen insularity perhaps I had better sit down

MILITARY PSYCHIATRIC CASUALTIES

EXPERIENCE WITH 12,000 CASES

HAROLD PALMER, M D MANC, M R C P, D P M
LIEUT-COLONEL RAMC

"In warfare the moral is to the physical as three is to one" *Napoleon*

TWO-THIRDS of psychiatric battle casualties are due to impaired or broken morale The successful rehabilitation of morale follows the principles of good "man management" Nevertheless it calls for specific qualities of skill, training, and experience which are only to be found in a psychiatrist

In these cases the will to fight, besides the capacity to fight, is impaired However, the term "psychiatric casualty" covers a class of military ineffective who is neither a deserter nor a coward, but should be regarded as a sick man with an illness of a different order from that usually met in our medical and surgical wards, where morale is not critically involved

Ætiology

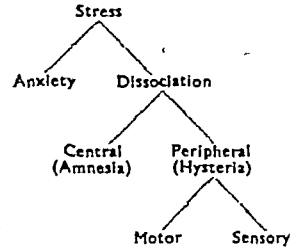
The psychiatric casualty is met both in static and in active warfare, whether pursuit, sustained attack, or retreat, and the clinical state varies somewhat with those conditions Enemy action provokes breakdown much more often than does the most intense physical discomfort. The incidence of psychiatric casualties roughly corresponds to the extent to which a unit is engaged, but is usually some 10% of all medical and surgical casualties The psychiatric casualty is rarely wounded, though it must not be assumed that the wounded do not sometimes show nervous symptoms On the whole, the type of man who deserts is not the type who appears in this group Officers are much less affected than other ranks

Most of these men have a hereditary constitutional predisposition to breakdown, with a history of previous minor neurotic traits and of emotional trauma in early life; hence they may be classified as insecure persons who have always been dependent on their families The precipitating cause often seems to have reactivated the pre-existing pattern associated in their subconscious minds with the previous nervous breakdown The most common precipitating cause is the real or imagined "near miss", the most common contributory factor is the death of a close comrade or platoon officer.

These men are connoisseurs in sincerity when being handled, so more often than not we are studying a reaction to handling as much as a primary reaction to danger and stress In a third of my cases the reaction to stress far outweighed in clinical and practical importance all other considerations; in the other two-thirds, besides some degree of incapacity, an unwillingness to fight was predominant In the first group the immediate cause of the man accepting the rôle of invalid is mental pain; in the second it is breakdown in morale, which is not necessarily a matter of the individual but may concern the group.

Classification of Syndromes

The following classification of battle reactions is based primarily on morale and includes four low-morale subgroups, classified as panic reactions, and four good-morale subgroups, classified as anguish reactions It is based secondarily on the quality of the response to stress. This response assumes either an anxiety pattern or a dissociative pattern, or a mixture of the two responses. Anxiety responses are never biologically protective, whereas dissociative responses often are Dissociative responses tend to assume one of two characteristic patterns the central are the amnesic syndromes, while the peripheral are the motor and sensory hysterias Further, the whole group is influenced by fatigue and privation, by the mode of handling before being first seen, and by the stage at which we first see them The descriptive groups shown above are compounded from a study of 12,000 cases, most of whom were battle casualties seen within 72 hrs. of the casualty and at an advanced general hospital



In all cases we are studying an equation relating combatant capacity—i e, the function which relates morale to constitutional endowment—to external stress

Suppose that a soldier is facing successive situations of increasing stress, and is equipped with a combatant capacity which is similarly increasing In the first syndrome we shall see him report sick fairly readily, and in the final syndrome we shall see him as a "burnt out" soldier succumb to his anxieties Somewhere along the series we shall begin to say that he is a sick man The criterion of his sickness is the degree of anguish or psychological pain he has suffered The objective sign of this pain is torpor I therefore distinguish panic reactions from anguish reactions The criterion of his morale is the readiness with which he accepts the rôle of invalid

Battle Reactions

PANIC REACTIONS

Panic reactions constitute 65% of my material and are induced by the sight of fear, pain, or death in others, or by thinking of them The soldier so affected has lost his power to control his emotional response. The reactions are reversible and subside without medical aid I therefore do not consider them as a true illness, they do not show any degree of torpor (These remarks do not imply any lack of sympathy, nor that I question the wisdom of evacuation or the scope for interference.) These panic reactions exhibit four subgroups, the first two being anxiety responses and the latter two dissociative responses

1. *Simple "Wind up" or Loss of Grip*—The soldier who is exposed to action must sooner or later experience fear or grief of a degree which he finds difficult to bear. These emotions may reactivate patterns of earlier mental experience and response At this point his behaviour is determined by his morale. If it is poor, he may cease to behave as an efficient soldier and may be a menace to the morale of his platoon, in whose interest he may be evacuated. This group constitutes 30% of my material, and is characterised by the disappearance of subjective or objective symptoms as soon as the men are out of sound of the guns Treatment should be immediate and well forward and consists of commonsense restorative measures, such as good sleep, hot meals, hot showers, and a change of kit Final disposal is based on an assessment of their combatant capacity A surprisingly high proportion of such men can thus be returned to duty It must be admitted that some will relapse, but this in no wise undercuts the justification or the proved success of such a policy The critical factors in handling this group are speed of attack, non-admission to hospital, and treatment well forward but just outside gun-range

2 *"Wind up" with Signs of Mild Anxiety: Scare.*—This group is somewhat artificially, but none the less usefully, separable from the first group by the fact that it consists of a somewhat better type of man who has stuck it out longer and in consequence is beginning to show signs of true anxiety, in so far as his reactions persist for a little time after his removal from danger He has been scared and shaken and requires more intense

and prolonged handling, even to the extent of a 3-day course of continuous narcosis. Such a man may conveniently be handled at the CCS, and final disposal, although depending on an assessment of combatant capacity, may in some cases await his passage through a forward rehabilitation unit. This group forms 15% of my cases.

The two groups which follow are both examples of dissociation. These reactions constitute the alternative reaction to anxiety, but this does not imply that the series of reactions are mutually exclusive or independent. Dissociative reactions are biologically purposeful and self protective, whereas anxiety reactions of the quality under discussion are neither purposive nor protective. These dissociative phenomena are otherwise referred to as the hysterias and contain two main subgroups, the amnesic and the motor-sensory syndromes. It must be assumed that in patients with these dissociative syndromes the threshold for dissociation is lower than the average for the community. The term conversion hysteria implies an acceptance of the Freudian psychopathology. Consistent both with such views and with other views is the simple assumption that dissociative features anticipate the graver types of anxiety response. The nervous system solves the patient's moral problem when exposed to danger by rendering him incapable of further action. In the low morale group under discussion the amnesic syndrome is very questionable, and I usually refer to the phenomena as 'false blackout.' Groups 3 and 4 constitute 20% of my cases.

3. *"Wind up" associated with Vague Features of Dissociation. False Blackout.*—At this stage the man is badly frightened and may show signs of terror. These signs appear either as aimless wandering or active screaming or crying or as complete incapacity. Unless given immediate treatment such men may develop all kinds of histrionic and regressive forms of behaviour. Abreactive and resynthesising techniques in combination with sleep treatment may be indicated, but above all the men must be treated with firm and vigorous persuasion in their own interests. Failure to handle them efficiently at an early stage may lead to various gross hysterical manifestations which may prove chronic therapeutic problems. The claim of blackout or amnesia requires careful scrutiny, and is characteristically claimed in excess of the truth.

4. *Simple Motor and Sensory Hysteria.*—This group is divided from the previous subgroup to draw attention to their prominent symptoms which are some loss of motor or sensory function. In the low morale series the dissociative mechanisms are only part of the total factors involved, and the loss of function is characteristically susceptible to rapid forms of reintegration by firm suggestion and persuasion. However, if they are allowed to stay untreated, all kinds of histrionic additions may develop. They must be carefully distinguished from the high morale hysterias. These conditions are to some extent "infectious," and this fact probably explains why they were extremely uncommon in the 8th Army, with its facilities for rapid treatment. In fact, I had never seen some of the syndromes described by certain authorities until I was called to deal with a batch of men in Italy who had been evacuated from Anzio before the inception of a forward psychiatric unit there, and had been left in an obscure corner of a general hospital.

None of the above groups is associated with torpor which is the safest objective evidence of the degree of mental pain existing. Where torpor is observed, we may assume the patient to be experiencing true anguish and to have been doing his best to control his anguish, and he can be classed in one of the following four subgroups.

ANGUISH REACTIONS

Anguish reactions constitute 35% of my material. They are beyond conscious control, are irreversible without skilled psychiatric interference, and have ceased to be topically determined. They are true illnesses. Morale is not critically involved: the cause of the patient's having reported sick being intolerable mental pain. In this sense the reactions are comparable with ordinary physical complaints. It is implied here that, where torpor exists, morale must have been average or high. Nevertheless, this relationship is not invariable, because though the torpor varies with the degree of anxiety, which in turn is usually connected with the state of morale, sometimes certain incidents may have a highly traumatic value for a given man at a stage of his military career at which his morale is still intact.

5. *True Battle Dissociative States. True Blackout.*—The soldier who is experiencing fear is in a highly receptive emotional state; and, if at such times he experiences a "near miss" sufficiently intensive to make him believe he is about to be killed, a massive protective response in the form of a complete "blackout" or dissociation of consciousness may be evoked. This interference with the stream of consciousness may be complete, so that he lies mute and still, or he may begin to sob. The more rapidly such a man is thoroughly reintegrated and abreacted the better. For these purposes ether may be indicated, and an opportunity should be given for emotional catharsis. This technique should immediately be followed by 24 hrs' narcosis. This group originally led to the term "shell shock," and represents 10% of all my cases. Some of these patients had blast injuries to the tympanum; therefore we cannot eliminate altogether the possibility of the existence of a true traumatic factor in this class of case.

6. *True Battle Anxiety Reactions.*—This group of men either lacks the inborn capacity to dissociate, or the capacity to do so has a high threshold, which for convenience we will assume has not been challenged by the experience of a "near miss." Moreover, the physiological accompaniments of anxiety, which are never primarily protective but are a form of preparedness for action, have ceased to have the exhilarating quality which they possess for the athlete or well trained soldier of good morale, and further have ceased to be topically determined, so that the reactions do not subside with the removal of the stimulus. Such a soldier sooner or later begins to find it difficult to master his anxiety signs and symptoms; hence during the whole 24 hrs. he is tense and in a condition of anxiety preparedness. He has a well marked startle reflex and a fine tremor, sweats excessively, and goes off his food and sleep. A vicious circle is rapidly set up, chiefly as a result of the loss of appetite and sleep, and his efficiency rapidly falls below the threshold of military requirements. He reports sick or is sent back and evacuated. Such cases are genuine and constitute true battle anxiety states. This is the man whom the Tommy calls "bomb happy." He should be regarded as a subchronic case, and if improperly handled *is very liable to develop features of secondary hysteria*, which are usually visceral in expression, but a particularly troublesome symptom is frontal headache. So wide spread was this headache in the ME that it became known as "Middle East headache" and appeared to have displaced effort syndrome from its former position of prominence. This secondary neurosis tends to chronicity unless vigorously treated.

The correct treatment for this group is continuous narcosis. Correctly judged abreactive techniques may be legitimately applied, but these are very dangerous in inexpert hands and may precipitate a true depressive illness. The course of sleep treatment should last 3-10 days according to severity; convalescence is fairly gradual and rehabilitation prolonged. Such men rarely acquire their former standards of toleration for noise and danger. Nevertheless, such a man, efficiently treated, who is possessed of high morale, may return to full battle duties. Such men must be regarded as very brave and must suffer from much anguish in so returning to duty. This group constitutes 15% of my cases.

7. *Pseudo-confusional Syndromes: Acute Battle Torpor.*—The man who is experiencing severe anxiety or grief may also be undergoing severe privation and fatigue. Many men in such circumstances experience a sense of "survival guilt." Approaching the end of his tether, such a man may experience a "near miss" or a situation which he cannot face. A massive diffuse dissociation takes place. These men are often found wandering, glazed, mute, and torpid, and are brought into the clinic in a bad physical state: severely dehydrated and often with a mild pyrexia. Where dissociation is not complete the picture is very like that of a tearful depression; such a man should be put to bed immediately and given plenty of fluids, an enema, and a sedative. The next day he must

be reintegrated with ether. Often it is necessary to use intense persuasion to shake such a man out of his torpor. This must be prosecuted with vigour, from which there is no danger, as this very genuine type of man is always an intensely grateful patient. Once he has regained full contact with reality and been given ample opportunity for a release of his pent-up emotions, he should be given narcosis treatment for 5 days. Convalescence should be prolonged to 3 weeks followed by rehabilitation. I never advise this type of man to return to full battle duty. This group constitutes the core of the problem under discussion, for whom the term "shell shock," though from an administrative point of view undesirable, nevertheless conveys to the minds of many an adequate sense of the mechanisms involved.

This syndrome simulates closely an acute schizophrenic reaction and is often so diagnosed. It is very difficult to diagnose other than from response to treatment in many of the cases. There is a very real danger of a depressive reaction supervening in such cases if they are not given an adequate course of sleep therapy. They constitute 3% of my cases.

8. *Severe Battle Motor Hysterias.*—We must now consider motor hysterias in men of high morale. This group is somewhat arbitrarily distinguished from the previous group, seeing that both groups may show severe degrees of torpor and anxiety, but the distinguishing feature is the existence of some prominent conversion phenomenon. On the whole the torpor of such cases is not so pronounced as in the preceding group. If a man is well trained and has high morale, he will continue to tolerate cumulative strain not only well past the breaking-point of the average man but also well past his own innate stability. In the end dissociative features may come to his rescue in the form of gross tremors, stammer, tics, or paralysis. It will be seen therefore that this group requires careful diagnosis from the low-morale conversion hysterias. The two groups only differ mechanically in respect of the level of consciousness at which dissociation has taken place. Consequently this group is harder to treat but, once treated successfully, tends not to relapse, so long as the men are not returned to forward line duty—i.e., so far as their behaviour in the ward is concerned, they are better clinical propositions. Moreover they do not exhibit regressive features and are likeable and grateful men. Treatment for all these cases is with ether followed by narcosis therapy. In giving abreactive treatment considerable care is necessary to establish therapeutic rapport. This group produces the most massive emotional catharsis during treatment and is characterised by having passed through the most harrowing experiences. They constitute 2% of my cases.

Campaign Reactions

9. *Campaign Neuroses.*—The average man, if exposed to prolonged stress, will sooner or later begin to show evidence of strain. There are examples of this reaction in the finest of soldiers; witness the effect of the retreat from Moscow on Marshal Ney, whom Napoleon described as the "bravest of the brave." These reactions, however, may declare themselves after a single exposure to prolonged severe stress, and in such cases there is a curiously regular latent interval of about 6 weeks before the onset of symptoms after the end of the prolonged stress. These symptoms are in general those of the anxiety states, to which may be superadded phobic obsessional features or features of personality deterioration.

These men gradually withdraw from effective contact with all but their closest chosen intimates, with whom nevertheless they derive much solace, churning up their sense of guilt of survival in the manner of the Ancient Mariner. Alcohol and feminine companionship will also be sought, and occasionally some absorbing hobby. The reaction is perhaps best understood in terms of ruminative grief, and its main physiological expression is overwork. To their friends they are seen to have "altered." They are ill at ease in company, especially with strangers, strive to avoid any stimulus to their emotions, and may show traits such as explosive anger or abnormal sexuality. Such men require prolonged psychotherapy, for which an initial course of continuous narcosis and very carefully judged abreaction may serve as a useful preliminary remedy, and they should not be discharged from the service until they have had a chance to rehabilitate themselves. Discharge from the service only adds to their sense of guilt.

Only a narrow dividing line separates such men from true depressive reactions. They do not develop major hysterical complications but do tend to hypochondriasis. These are undoubtedly conversion phenomena. The average well-trained soldier is likely to show signs of stress after 5 days of intense day-and-night fighting, and after 2 years of active service overseas. In practice the soldier will often date his demoralisation from a particular incident, such as the evacuation from Dunkirk, the sinking of the *Lancastria*, the evacuation from Crete, or the desert battles of November, 1941, to February, 1942. This tendency, however, may simply be a form of projection, the mechanism of which is most commonly seen in the neurotic who attributes all his troubles to a head injury. The campaign neuroses here described link up with the true battle anxiety reactions, and the cases of "wind up" with signs of mild anxiety as a continuous series with evidence of greater or lesser degree of habit-formation. They constitute 5% of my cases.

Miscellaneous Syndromes

The nine syndromes described above include all the amnesic syndromes; it has now been generally recognised that the claim of loss of memory is one which at all times should be accepted with the greatest reserve. Nevertheless any man may establish unfair prejudice against himself by his exaggerated claims, and in most instances, especially where disciplinary action is involved, we must consider the initial period of 15 min. to 2 hrs., which is often genuine. A subsequent period of a few hours ensues, in which reintegration is taking place, during which it is extremely difficult to assess moral responsibility, and a final period may develop during which there is frank malingering. Under ether these 3 phases will rapidly declare themselves. Ether is also an indispensable diagnostic technique in distinguishing the functional, the traumatic, and the schizophrenic case. The epileptic reacts like the traumatic. It is necessary to distinguish between the three broad divisions of men: those whose reactions are under conscious control, those whose reactions are on the borderland of conscious control, and those whose reactions are not consciously controlled.

No detailed remarks on psychotic syndromes are offered. The importance of not mistaking certain severely dissociated patients, who can be reintegrated in a few hours, from true schizophrenics has been mentioned. True psychotic syndromes formed not more than 2% of my material. It has often been alleged that exposure to military stress is not a cause of psychosis. I do not agree with this statement. There exists an acute paranoid state, with a good prognosis, characterised by visual and auditory hallucinations. This condition has to be distinguished from acute hysterical reactions in high-grade defectives and does not include fugue-like states met with in schizophrenics, which can be cleared up with ether.

Symptomatology

In describing my nine syndromes very little mention has been made of specific symptoms. These can be classified as follows:

Primary Symptoms of dissociation, or anxiety, or both:

Lack of concentration	Tics
Amnesia	Disturbance of special senses
Torpor	Motor disturbances
Pseudo-torpor.	Sensory disturbances
Stammer	
Diffuse anxiety and/or Depression	Lassitude.
Insomnia	Emotional instability.
Battle dreams	Feelings of unreality
Headache	Irritability
Dizziness	Hypersensitivity
Visceral disturbances	Fatigability

Secondary Hysterical Elaboration of Primary Features.—These lead the patient to believe that he is a sick man. They constitute prolongation syndromes, which may in turn develop into fixation and hypochondriacal syndromes. Such a condition once installed is often labelled "anxiety state."

Tertiary Hysterical Formulation of Subjectively Felt Incapacity to Fight.—These features, more or less consciously formulated by the patient, constitute the main task of the military psychiatrist, which can be achieved only within the frame work of a military rehabilitation centre. Prolonged stay in hospital over 21 days is nearly always harmful.

Quaternary Conscious Formulation.—"I won't fight, because the Army has no right to expect me to." This may be rationalised further as "I've done my bit, now let others do their bit," or "I would be of no use to my unit and would only break down again" or "I never was an A1 man," and so forth. Treatment is entirely by rehabilitation.

Personality Reactions.—These include compulsive features, alcoholism, abnormal sexuality, paranoid formulations, and chronic anxiety reactions. Treatment of these reactions requires prolonged and skilled psychotherapy in a base unit. They do not respond well to rehabilitation, but on the contrary require prolonged convalescence. Above all other conditions met with in this field, they are a specific field for the occupational therapist.

Symptomatology is only referred to briefly. We are not primarily concerned with treating symptoms, but with treating the patient and his disease. This disease is the soldier's belief of incapacity to fight, which may become a quaternary formulation—"I won't fight"—in faultily handled cases. In all our cases we must try to find why the man has accepted the rôle of invalid. This amounts to assessing his morale before his breakdown, together with the degree of anguish involved. Much of our treatment is concerned with handling the patient's concept of himself as a sick man in relation to our concept of him as a soldier with a further duty to his comrades. The psychiatrist must therefore resist the soldier's attempt to convert the real problem into a discussion between him and the psychiatrist about his symptoms. Such an attitude is harmful to the patient and produces a hot-house atmosphere in any clinic in which it is encouraged, which *militates against* the principles laid down here.

Psychopathology

If my thesis is correct, the underlying pathology is the psychopathology of demoralisation. The psychiatrist may, however, study the problem at any level of functional integration of personality which his interests dispose him to select. Demoralisation provides a field for very extensive study, which I do not feel competent to discuss. I nevertheless draw attention to the following *contributory factors*.

1. Fatigue or privation may have undermined the soldier's real or imagined capacity to carry on. This is what the soldier means when he says he is 'played out,' "fed up" or 'browned off.'

2. The physiological accompaniments of stress have caused the soldier to feel that he cannot carry on. The signs of anxiety may or may not have passed the normal threshold which any soldier experiences, but, when they have done so, they tend to assume an automaticity and persistence of response sufficient to justify the term "anxiety state." When this happens, the soldier's comrades refer to him as 'bomb happy.' It is a condition of permanent 'wind up.'

3. A dissociation may have been induced which varies from a massive incapacitating loss of function, for which the soldier is in no way morally responsible to a minor degree of dissociation which the soldier elaborates more or less consciously as a means of justifying his "throwing in the sponge." The modern soldier refers to these phenomena as 'blackouts' and where the original 'blackout' has arisen in relationship to a near or fancied "near miss" we have the origin of the term 'shell shock.' A distinguished clinician called these three groups 'fed up,' 'wind up' and 'blown up.'

Other factors are mentioned in the discussion of prophylaxis (see below). Dominating all these factors are the importance of good leadership, the shock attending the loss of the boon companion, the importance of a sense of good support from all ground and air arms, and the sense of superiority in weapons.

It is perhaps not out of place to mention that in my experience the British Tommy has never regarded the enemy as his equal as a fighting man, though admiring his courage and discipline on many occasions, and he has confidence in his leaders, as shown by his respect for his officers and NCOs. Although inclined to criticise welfare arrangements, he has characteristically vented his grouse on the climate or commercial morality of the inhabitants of the country in which he has been campaigning.

In discussing the psychopathology of such a heterogeneous group of syndromes it is very difficult to present a psychopathology which can be applied to the whole series, hence a complete grade of cases will be met, from the man in whom the loss of morale is the sole cause of a breakdown to the man whose bravery is not to be questioned. In this latter group attention has already been drawn to the ruminative grief associated with a sense of guilt of survival.

Finally the symptom of torpor demands further study. This torpor has been noticed by several writers, and Gillespie[1] has drawn attention to the condition of accidie, as recognised by the early Christian Fathers, quoting St. John Damascene. The condition is not to be confused with apathy but more probably represents the inhibited emotion associated sometimes with anxiety, which so easily tends to pass over into a state of depression.

Prophylaxis

I questioned 150 men about which factors promoted and which impaired their morale. The factors promoting morale were said to be first and foremost the qualities of leadership in the officer, followed by such obvious factors as adequate rest periods, good support, rations, sleep, physical well being, knowledge of the tactical plan, and reassurance that the task in hand was well within their capacity. The Tommy appears to respect high standards of discipline on parade but dislikes spit-and-polish on other occasions. Bad leadership, no news from home, a sense of inferiority in weapons, bad support, and, curiously enough, a sense of inadequate medical arrangements were all mentioned as adverse factors. It appears that the death of his MO is more immediately symbolical of insecurity than any other single factor.

It has often been said that there are no bad soldiers but only bad officers. I venture the suggestion that the weakest link in the British Army's machinery is the relative neglect of the junior NCO. It seems to me that a man does not begin to feel himself responsible for morale until he has received his third stripe.

Prophylaxis therefore consists in:

1. Selection of recruits in conjunction with personnel selection officers (PSO).
2. Selective posting.
3. The education of combatant officers in the principles of good man management.
4. The training of all RAMC personnel in the correct methods of handling psychiatric cases.

Lying behind all these considerations is good management. This term is not synonymous with, but nevertheless includes, what is usually called welfare.

(To be concluded)

1. Gillespie, R. D. (1943) Psychological Effects of War on Citizen and Soldier. New York, p. 80.

THE *Third Handlist of Recent Medical Films* just published by the Scientific Film Association, lists another twelve good films, divided as before into two groups—Direct Teaching and Background. Four films completed only within the last month or two are detailed, as well as an amateur film not previously available and two films prepared by the Services. This indicates that the SFA are obtaining recognition of their policy for making medical films available more widely. The list is available from the hon. secretary of the Scientific Film Association, c/o The Royal Photographic Society, 16, Princes Gate, SW 7.

THE synthetic vasoconstrictor "Privine" made by Ciba Ltd., is now available in this country in isotonic solutions of 1 in 1000 or 1 in 2000 for application to the nasal mucous membrane. Privine is 2-(naphthyl 1 methyl)-imidazoline hydrochloride. Its decongestive action is said to last 4-6 hours. The makers recommend that the dose should be restricted to 2-3 drops in each nostril and that treatment should not continue for more than 4-5 days at a time.

HEPATORENAL SYNDROME TREATED WITH CHOLINE CHLORIDE

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IN 1939 Griffith and Wade noted hæmorrhagic degeneration of the kidneys in young male rats fed on an alipotropic diet Subsequent work by Griffith (1940, 1941), Christensen (1940), and Gyorgy and Goldblatt (1940) showed that these changes were reversible and preventable with choline. Beattie (1944) has reported the beneficial effects of choline on kidney failure associated with severe liver damage in man In view of the importance of this observation, we are reporting a successful result in a man whose clinical and metabolic state was such that death was thought to be inevitable

CASE-REPORT

A man, aged 27 years In childhood he had a mild jaundice for two weeks Otherwise he was healthy, playing games vigorously, including boxing and Rugby football, until the time of his entering the Army, in category A1 There was no family history of jaundice

On July 17, 1944, he was admitted to a field dressing station in a severe anxiety and exhaustion state He was given gr 60 of soluble barbitone over 5 days, but he was still depressed, apprehensive, and self-reproachful During the next 3 days he received phenobarbitone gr 4, and in the next 2 days, immediately before admission to a Neurosis Centre on the 26th, he was given soluble barbitone gr 30 and 'Sodium Amytal' gr 18 When admitted at 7 PM he was deeply unconscious, incontinent, with temperature 99° F, pulse-rate 120, respirations 22 per min Corneal reflexes, and knee- and ankle-jerks absent BP 70/? mm Hg No urine was obtainable Picrotoxin 2 c cm was given hourly, and after four doses he returned to consciousness

July 27: passed 3 stools containing blood and mucus, and vomited six times BP 130/90 No urine was passed

July 28 restless with severe abdominal pain, vomiting, and hiccup Dysentery was considered possible, so he was given sulphaguanidine 18 g by mouth over 22 hours and 3 pints of glucose-saline intravenously Blood urea 20 mg per 100 c cm Red cells 6,260,000 per c mm Hb 94%. White cells 7600 per c mm No urine passed

July 29 still vomiting Skin of abdomen jaundiced. Transferred to Queen Elizabeth Hospital under Prof W H. Wynn At 3 PM conjunctivæ and skin jaundiced, drowsy and uncooperative, tongue moist and coated, chest clear, BP 130/70, pulse 72, good volume, generalised abdominal tenderness, liver and spleen not palpable, knee- and ankle-jerks present with flexor plantar responses, arm reflexes absent. At 6 30 PM severe hiccup, speech slurred, stools almost pure blood, Hb 86% No urine passed

July 30 hiccup continually present with much nausea and vomiting of bloodstained fluid Taking fluids well. Still very drowsy Urine 2 drachms (containing moderate albumin with few red and white cells, no casts)

July 31 persistent hiccup and vomiting Stools loose, consisting of blood and mucus Continuous intravenous glucose and saline drip started Blood-urea 146 mg, serum bilirubin 3 2 mg per 100 c cm Choline 2 g given by mouth Vomit 34 oz No urine passed

Aug 1 still vomiting bloodstained fluid Severe hiccup Jaundice deeper Bowels opened 8 times during the day. Given choline 5 g by mouth and 2 g at 6 PM in the dextrose and saline drip, covered by atropine gr 1/75 six-hourly No urine passed

Aug 2 · at 9 30 AM passed 4½ oz of urine Still vomiting Bowels frequently opened with very bloodstained motions Rather drowsy and moderately jaundiced Some headache and severe hiccup Passed 2½ oz urine at 4 PM, and further 1½ oz at 8 PM Blood-urea 255 mg per 100 c cm Plasma CO_2-combining power 36 vols. % Serum bilirubin 16 mg per 100 c cm Choline 8 g. given by intravenous drip Vomit 41 oz Urine 8½ oz (containing moderate albumin, and red cells)

Aug. 3 hiccup continued most of the day with the patient sleeping between the exacerbations Diarrhœa controlled with passage of first formed motion without blood, but very offensive. Asked for eggs and bread and butter, which he ate and enjoyed. Blood-urea 290 mg, serum bilirubin 21 3 mg per 100 c cm Plasma CO_2 33 vols. % Hartmann's solution substituted for dextrose-saline Choline 8 g given by intravenous drip Vomit 17½ oz. Urine 14½ oz (containing no albumin)

Aug 4. hiccup still very troublesome More jaundiced Liver palpable, well below costal margin Much abdominal pain and distension Bowels open only once Developed irritating generalised macular rash Sodium citrate and citric acid mixture[1] given by mouth to counteract acidosis, in addition to Hartmann's solution Methionine substituted for choline Blood-urea 300 mg., serum bilirubin 18 25 mg per 100 c cm. Plasma CO_2 30 vols. %. Choline 6 g and methionine 4 g given by intravenous drip Vomit 10½ oz Urine 34½ oz (no albumin)

Aug. 5 hiccup persisted Drowsy and not taking anything except fluids Slight recurrence of diarrhœa, but no blood. Blood-urea 340 mg per 100 c cm Plasma CO_2 25 vols % Given methionine 6 g and Hartmann's solution by intravenous drip Sodium citrate and citric acid by mouth Vomit 12 oz Urine 65 oz

Aug. 6 still drowsy with dark urine and soft clay-coloured stools Rash very irritating. Liver smaller Hiccup still occasionally troublesome Enjoyed tea for first time and had jam sandwiches Bowels opened only once Hartmann's solution by intravenous drip, sodium citrate and citric acid by mouth. Urine 91 oz

Aug. 7 taking citric acid mixture well Liver back to costal margin Bowels open twice with good deal of mucus Blood-urea 285 mg per 100 c cm Plasma CO_2 50 5 vols % Serum bilirubin 21 mg per 100 c cm Red cells 2,850,000 per c.mm Hb 58% Hartmann's solution given by intravenous, drip Urine 100 oz

Aug 8 now beginning to take solid diet and smoked for the first time Still very jaundiced Blood-urea 268 mg, serum bilirubin 18 3 mg per 100 c cm Plasma CO_2 53 vols % Given Hartmann's solution by intravenous drip. Urine 90 oz

Aug 9 intravenous drip discontinued Patient's chief complaint now abdominal colic and distension.

Aug 14 methionine 10 g given by intravenous drip in 500 c cm. of normal saline Red cells 2,700,000 per c.mm. Hb 54% Blood-urea 165 mg, serum bilirubin 4 65 mg per 100 c cm BP 130/90 mm Hg

Aug 15 feeling extremely well, taking high protein and carbohydrate and low fat diet

At this stage the patient was excreting as much fluid as he took in He had become anæmic Liver extract 4 c cm was given with only a moderate reticulocyte response. He still looked jaundiced and complained that his face was puffy,

1 Sodium citrate 98 g, citric acid 140 g, water to 1000 c.cm

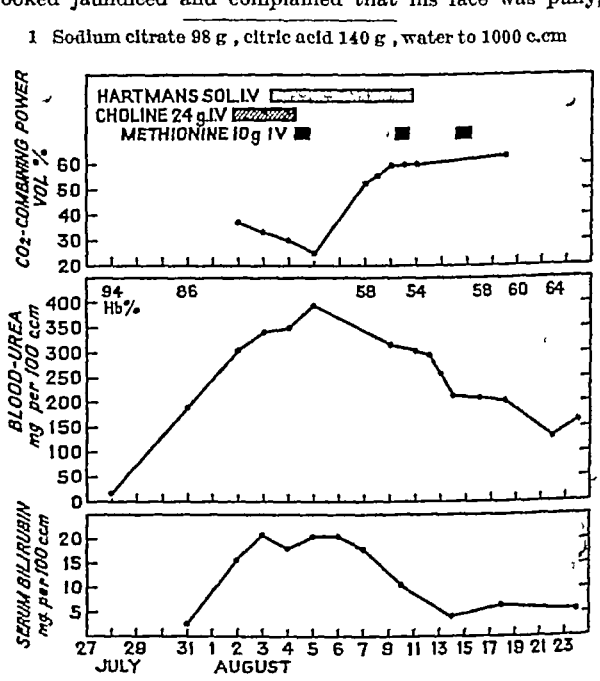

Fig 1—Blood findings Choline was given by continuous drip Note time scale alteration after Aug 7, 1944

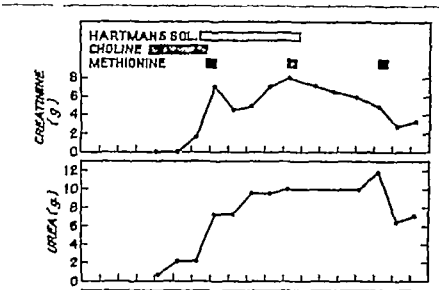

Fig 2—Urinary excretion and fluid intake. Choline 24 g intravenously by continuous drip Methionine intravenously in 10 g doses. Hartmann's solution given intravenously White columns denote water intake. Black columns denote urine output.

though no œdema was detectable On Aug 10 he weighed 9 st 8 lb and within the next few days he developed a well marked diuresis his face rapidly became thinner and from appearing rather plethoric and podgy he became a slim

URINARY EXCRETION PER 24 HOURS

	Aug 2	Aug 3	Aug 4	Aug 5	Aug 6	Aug 7	Aug 8
Chloride (g)	0 580	1·6	1 8	8 °	8 3	7·6	–
Phosphate (g)	0 021	0 142	0 163	0 574	0 445	0 566	0 688
Creatine (g)	0 027	0 158	0 170	0 288	0·223	0 176	0·288

athletic looking young man—so that on Aug 20 he weighed 8 st 5 lb At about the same time as his diuresis he developed a ravenous appetite Thereafter the patient felt in excellent health, but his metabolic studies were slow in returning to normal and a further dose of methionine (10 g) and finally choline (8 g) was given to produce the final fall in blood urea On Sept 10 inulin-clearance was 80 5 c cm per min (normal 100–120), diodrast-clearance 662 c.cm per min. (normal 600 700), and renal blood flow 1050 c cm (normal 1200–1500) with Tm I_2 (diodrast) 22 mg per min (normal 40–60)

Nocturnal frequency cleared up a week before his discharge from hospital on Nov 9 Physical examination then was negative Weight 8 st. 6 lb BP 145/90 mm Hg Red cells 4,670 000 per c.mm Hb 90% Blood urea 39 mg., serum bilirubin less than 0 2 mg per 100 c.cm. Colloidal gold test 33210

The outstanding points in the illness are the concomitant rise of blood urea and serum bilirubin increase of acidosis, and partial restoration of kidney function (figs. 1 and 2) The electrolyte patterns (fig 3) show the additional feature—increase of organic acids paralleling the increase of blood urea As will be seen in fig 1 haemoglobin underwent a rapid fall during the acute stage of the illness and in spite of weekly injections of crude liver extract was only 70% on Sept 20 Serum cholesterol at the onset of illness was 205 mg. per 100 c cm rising to 304 mg seven days later, and thereafter falling gradually to 115 mg shortly before discharge

DISCUSSION

The cause of the failure of liver and kidney function in this patient is obscure The previous attack of jaundice probably rendered him more liable to a severe attack of hepatitis of any aetiology In view of its prevalence the possibility of a coincidental attack of infective hepatitis cannot entirely be ruled out Weil's disease is also endemic on the Western Front, but the absence of any sustained fever and leucocytosis seems to be against this diagnosis We have not found any record of picrotoxin causing severe liver damage Jaundice and hepatic degeneration have been described in barbiturate poisoning and some of these cases have had renal damage (Sollmann 1942), and though liver damage of the degree seen in our patient is rare in barbiturate poisoning, this seems to be the most likely cause

The initial finding of a blood urea of 20 mg per 100 c cm on the second day of urine suppression, and 140 mg with a serum bilirubin of 3 2 mg on the fifth day, suggested that liver function was almost completely suppressed The subsequent rapid alteration with therapy emphasises this

In spite of rapid return of urine output the blood urea continued to rise, and a probable explanation is that the deamination power of the liver was then relatively greater than the kidney clearance That kidney function was still very depressed can be seen from the creatinine excretion on Aug 6, when the clearance was approximately 25 c.cm per minute The increase in the organic acid residue (fig 3) is further evidence that liver function is exceeding the rate of recovery of the kidney This type of picture usually indicates a fatal outcome

As will be appreciated from the case history, the patient was critically ill with cholaemia and kidney failure at the time choline therapy was instituted From fig 1 it seems justifiable to conclude that choline was the causal factor in the restoration of kidney and liver function, which started within 12 hours of its initiation That there was a probable lipotropic effect was demonstrated by the fall in CO_2 combining power, the excretion of acetone bodies in the breath, and the rise in organic acids, due presumably to the liberation of fat from the liver Furthermore as was shown by the inulin and diodrast clearances kidney function subsequently underwent a gradual and constant return towards normality and, with the gradual fall of serum bilirubin, the same is true of liver function

The rôle of methionine is difficult to assess The patient received 30 g in divided doses in the ten days following choline The first dose did appear to coincide with a further small improvement in creatinine clearance and fall in blood urea and with a pronounced increase in total and neutral sulphate Subsequent doses had no

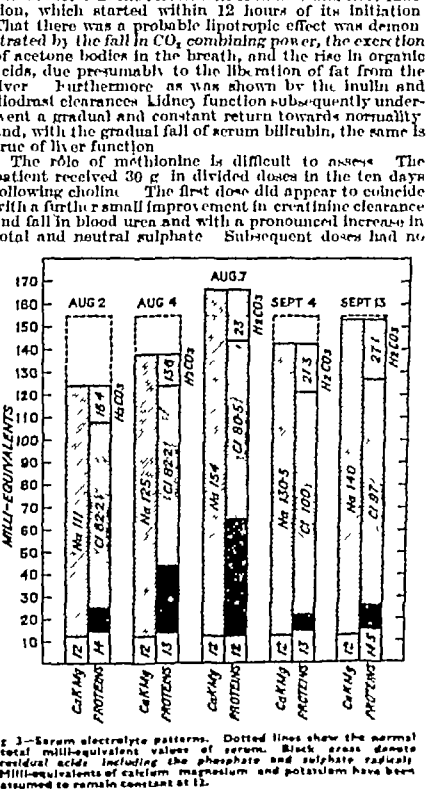

Fig 3—Serum electrolyte patterns. Dotted lines show the normal total milli-equivalent values of serum. Black areas denote residual acids including the phosphate and sulphate radicals Milli-equivalents of calcium magnesium and potassium have been assumed to remain constant at 12.

definite effect either on the metabolic picture or on the gradual return to clinical normality.

We do not feel justified to comment further on the changes in excretion of sulphates, chlorides, phosphates, and creatine.

The well-marked fall in hæmoglobin might have been expected in view of the severe liver dysfunction The response, however, to crude liver therapy was not striking —indeed it is doubtful whether there was any real effect The second dose of choline was associated with a slight fall in hæmoglobin, and according to Davis (1944) choline itself produces an anæmia It is not inconceivable, therefore, that choline therapy was the primary cause of the fall in red cells

Two points of clinical importance deserve emphasis Intravenous choline therapy causes severe sweating, bronchial secretion, and painful abdominal cramps For this reason it is dangerous in severely ill patients unless the bronchial secretion can be prevented We used atropine in fairly large dosage At no time was there any evidence of lung œdema, though the skin was moist Abdominal cramps were not troublesome during therapy, and the subsequent distension and abdominal colics appear to be similar to those seen in the recovery stages of some hæmorrhagic diarrhœas On the third day of choline therapy the patient developed a diffuse *macular* rash over the trunk, arms, and thighs, which was slightly irritating It disappeared within 72 hours of ceasing the therapy No side effects were noted with methionine.

SUMMARY

A soldier, aged 27 years, developed severe hepatorenal failure after receiving large doses of barbiturates for anxiety state.

Treatment with intravenous choline, followed by methionine, resulted in recovery

We wish to thank Professor Wynn for permission to publish this case, and Sister B. Whitehead for her careful supervision and nursing

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SIGMOIDOSCOPY IN AMŒBIC DYSENTERY

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THIS paper is written to stimulate closer and more accurate study of the bowel lesions in amœbic dysentery The disturbing incidence of chronic bowel disorders in personnel returned or returning from the East demands from the profession as a whole a high order of competence in the handling of the dysenteries; the consequences for the patient and his or her immediate associates of inadequate diagnosis and treatment of amœbiasis are grave

At the outset it must be emphasised that, from the standpoint of diagnosis and response to treatment, amœbic dysentery presents itself in two strikingly contrasted forms—the fresh acute case, and all other types of case This latter non-acute group comprises the chronic, the recurrent, and the "low growling" types; its numbers are swelled by the many who remain long undiagnosed because practically symptomless

In the fresh acute case diagnosis by the routine stool test, carried out on admission in all dysentery wards, is quick and easy, and the prognosis is good As a diagnostic aid sigmoidoscopy is both unnecessary and (because painful) contra-indicated. There are few exceptions to this rule Vegetative *Entamœba histolytica* will almost certainly be reported on the first or second day

But other types of case are bafflingly hedged about with doubt and difficulty, and the approach to them is beset with pitfalls A considerable degree of expertness and experience is essential in the identification of cysts, repeated stool examinations are necessary, and efficient organisation of stool tests on a large scale with shortage of hospital staff is by no means easy. Moreover, in my experience, many patients with stools reported as "normal" or "indefinite exudate only" come to light as cases of amœbic dysentery solely as the result of sigmoidoscopy Added to this is the difficulty that constipation is a not infrequent feature of recurrent amœbic dysentery, which further militates against a rapid laboratory diagnosis

Not only does sigmoidoscopy avoid delay in treatment in the non-acute case, but also it furnishes an important base-line for comparison with later sigmoidoscopies

But sigmoidoscopy has its limitations, and there is no doubt that sigmoidoscopy sometimes gives a negative result when there is active infection higher in the bowel If this point be kept in mind, the value of sigmoidoscopy will be kept in its true perspective In connexion with this, it is somewhat significant that the maximal incidence of the commonest lesion of amœbic dysentery (the pin-point crater described below) is 3–6 in from the anus Indeed, in over 500 sigmoidoscopies this lesion has never been observed so high as the point where the internal iliac artery can be seen pulsating against the sigmoid—i e, about 7½ in from the anus This suggests that the organism has, by happy accident, a selective action in many cases on that part of the colon directly visible to the physician

In the non-acute case the sigmoidoscope is so valuable that, besides cases with frank diarrhœa, the following classes of patients who have lived in the tropics should be examined sigmoidoscopically

(1) Cases of sprue
(2) Any case at all suggesting amœboma of the bowel or pulmonary amœbiasis
(3) Refractory cases of allergic disease, gastritis, and headache
(4) Hepatomegaly and suspected liver abscess
(5) Unexplained loss of weight

So protean are the symptoms of amœbiasis, and often so slight, that mass sigmoidoscopy of all personnel from the tropics would be the counsel of perfection

Enthusiasm for sigmoidoscopy should not lead to its being overdone, it should never be carried out without logical indication For instance, at the end of a course of treatment it is well to defer this examination for 3–4 weeks if the patient is symptomless, for it has been found that lesions which were present at the end of a course of treatment often disappear in a few weeks without further medication, suggesting that the standard treatments have a cumulative effect

CHOICE OF INSTRUMENT

Often a proctoscope will give as much information as a sigmoidoscope But it is in general wise to adhere to the one instrument, for the distance to which instrumentation is possible or desirable will always be a matter of trial, and the proctoscope has no advantage over the sigmoidoscope for purely rectal examination

The instrument of choice is the plated sigmoidoscope of about 11/16-in diameter with proximal lighting, the average magnifying lens giving a magnification of 4–5 diameters This size is highly satisfactory for the examination of either sex.

THE NORMAL MUCOSA

Before describing the lesions of amœbic dysentery visible with the sigmoidoscope, it is convenient to establish a clear conception of the normal mucosa Any deviations from this, if corresponding to the lesions enumerated, are to be regarded as evidence of infection.

The healthy mucous membrane, on close inspection by the stroking method described below, greatly resembles the surface of satin; it is not amorphous but a composite surface built up of just-visible gland-mouths There is an occasional wrinkle over an underlying venule. This, and only this, can be passed as normal Sigmoidoscopy reports not infrequently lay stress on "excess of mucus" or "some inflammation," but these are irrelevant points often depending on the mode of preparation and the patient's susceptibility to it

TYPES OF AMŒBIC LESION

The lesions described, if not actually amœbic in origin, which they almost certainly are, can accurately be referred to as "commonly associated with amœbic dysentery" In tropical practice any patient who has passed blood in the stool and at some later date complains of one or other of the symptoms of amœbic dysentery, however protean, will as a general rule exhibit lesions

In describing the appearances seen it is impossible to be dogmatic in labelling one or other of them acute or chronic, for in a disease whose onset is so disquietingly insidious, and whose symptoms are so misleadingly protean, the duration of infection is never free from the element of doubt

Classical ulcers —These present an infinite variety in size, shape, and distribution, varying may be from two small areas, ¼ in. across, at 5 in from the anus to almost total obscuration by ulceration, blood, and pus of the normal mucosa 2–8 in. from the anal margin

The "unit of ulceration" is the classical flat shallow depression with undermined congested edges and irregular contour tending often to a diamond shape The slough covering the floor varies in consistence and in degree of staining with pus, blood, and facal matter; most characteristic is a yellow purulent leathery membrane with bright blood oozing scantily from its cracks and edges. The bowel therefore bleeds easily on instrumentation, and a bloodstained discharge may escape from the tube as the obturator is removed

One might go so far as to say that some 40% of presumably acute cases, passing vegetative forms, will show from one to three ¼-in classical ulcers between 3 in and 6 in It would be misleading to make any more definite statement than that The remainder will show grosser ulceration or various numbers of pin point craters.

There is no correlation whatever between the duration of infection and the severity of symptoms, on the one hand, and the extent of ulceration In an intelligent nursing orderly, long experienced in the nursing of this disease, who presented no symptoms beyond occasional looseness of the bowels, and in whom sigmoidoscopy was done as an almost excessive precaution, the last 6 in of mucosa presented nothing but gross destructive shreddy ulceration; sigmoidoscopy was not painful

The valves, particularly their free edges, may be involved with or without other parts of the visible bowel

The classical ulcers are quite characteristic and unmistakable They respond with great rapidity to emetine If re-examined on the 4th or 5th day of treatment, the mucosa usually reveals an almost magic transformation-scene; great areas of gross slough will be found to have been removed, exposing normal mucous membrane dotted here and there with larger or smaller colonies of pin point craters in the average case

Yellow-headed ulcers —These are a subvariety of the classical ulcer being a bright shiny homogeneous slough covering in the ulcer floor and resembling a pustule about to break down. Sometimes they are widely scattered and extensive; sometimes the only evidence of infection consists of two small (¼-in.) circular "pustules" at perhaps 6 in, the remaining mucous membrane having an entirely normal appearance They usually respond readily to treatment.

Pin point craters —It has been seen above that the healing classical ulcer generally leaves behind a colony of pin point craters. I have used this term to indicate the minute central dark dot which, surrounded by its heaped edge, constitutes the small circular structure so commonly found in amœbic dysentery

These craters, just visible without the magnifying lens of the instrument, can only be readily detected by the stroking method described below Oblique illumination shows them up as strikingly reminiscent of an aerial photograph of bomb craters on an airfield; they have also been likened to photographs of the craters on the surface of the moon

The average diameter of a whole crater is about 1–2 mm., but they may be bigger or much smaller With a tube of ⅝ in diameter some 3–8 craters will be seen in one field They are most generally distributed 3–7 in from the anus; the valves are often affected, the free edge of one valve often showing a single crater They may be so few as to take a minute or two to find; perhaps two colonies of 5 or 6 craters at 6 in are the sole evidence of infection On the other hand, in many a case the whole visible bowel is peppered with small craters; in such cases there is attendant congestion and granularity affecting the mucosa generally, but when the craters are few the intervening mucosa appears normal

The colour of the craters is the same as that of normal mucosa though somewhat paler. The consistence is definitely warty, the manipulator being able to feel the tube slipping over the larger craters One would thus not expect scrapings to yield pathological evidence of interest, and this is in practice the case

Final evidence of the craters being specifically amœbic in origin is extremely difficult to obtain, but I am convinced, from several hundreds of cases, that their presence may, as a working hypothesis, be taken to indicate the existence of active amœbic infection Certainly they do not represent a final stage of healing or scarring It is very desirable that further evidence of aetiology should be obtained from the sectioning of pin point craters found post mortem in patients dying from causes other than dysentery, in the past, attention has been too narrowly focused on the pathology of fatal cases of amœbic dysentery, but the lesions of fulminating amœbiasis form quite a separate study from those of the non-acute type which cause such widespread chronic invaliding

It is a remarkable fact that the standard works on the dysenteries make no reference, so far as can be ascertained, to these craterform lesions.

Although the craters have in many cases been seen to disappear, they are in the main very refractory to the standard treatments. They thus bear one of the hallmarks of chronic amœbic dysentery

The disappearance of the craters is most often noted when they follow an acute attack with vegetative amœbæ in evidence or in mild non acute cases In the process of healing they become gradually smaller, losing the central pin point depression and resembling flat-topped cutaneous warts before finally disappearing

Pigskin appearance —This name, suggested by Major R. Kemball Price, is highly descriptive A number of cases present a mucosa normal except for minute scattered pits, such as might be produced by pinpricking a 'Plasticine' surface Pigskin appearance may be seen in association with classical ulcers pin point craters, or following the disappearance of either there can be little doubt of its amœbic nature It is very persistent but has been observed to disappear in rare cases.

Granular surface —Granularity of the surface of the mucosa intervening between ulcers or craters is often seen; probably amœbic in origin, it has little special significance and recovers pari passu with the accompanying lesions.

Healed amœbic ulcers —In many a case that has been diagnosed early and fully treated all lesions disappear leaving no trace; the satiny mucosa is completely restored. Other successfully treated cases show, on close inspection, slightly depressed glistening areas where the original ulcers existed They are yellowish pink and devoid of mucous glands

In certain very chronic intractable cases the mucosa gives a devitalised pickled impression, the colour tending to mother-of pearl, the valve edges being blunted and scarred

Artefacts —With care and gentleness the lip of the sigmoidoscope will rarely injure the mucosa When this does happen a semicircular cut or more extensive abrasion results. This does no harm but causes unnecessary pain A further reason for avoiding such traumata is that they confuse the issue by greatly resembling the isolated bleeding areas seen in some cases of bacillary dysentery

TECHNIQUE

With correct technique and in the absence of piles, acute proctitis, &c, sigmoidoscopy is a painless and very minor procedure Wide divergencies of practice exist at present The technique recommended is as follows

Sigmoidoscopy room —The atmosphere of the operating theatre is to be studiously avoided. It is essential that the reputation of sigmoidoscopy among the patients in the dysentery ward should be that of a trivial and

unalarming procedure, which indeed, if properly carried out, it is. The most evident reason for this is the annoying degree of spasm, greatly interfering with easy and painless examination, which develops in the nervous case.

A soldier patient recently invalided from India describes his subsequent experiences as follows: "The preparation for the sigmoid was a lot different to India. There I was starved for two days. I had two soap enemas and washouts. On top of that they shaved me back and front, and to top it all they carried me to the operation on a stretcher." Comment is superfluous.

Ideally the room used should be situated at one end of the dysentery ward. There should be a waiting-room attached, where a matter-of-fact atmosphere is engendered by the provision of light literature. Sigmoidoscopy is carried out on a wooden table 3 ft. long, 3 ft. wide, and 3 ft. high, covered with 4 layers of blanket, a sheet, and a towel.

Preparation of patient.—If sigmoidoscopies start at 9.30 AM., enemas are given as follows:

7.30 AM.	half-strength soap enema
8.00 AM.	2½% sod. bicarb. enema

This method is found to give almost 100% clean preparation, and no restrictions or elaborations are called for, except that breakfast should be dry and light. Additional washouts not only render the preparation less effective but also are an unnecessary ordeal for the patient.

Sedation is contra-indicated. There could be no greater error in technique than the giving of morphine.

Position of patient.—This should be genupectoral in either sex, unless the patient is too weak, in which case the left lateral is best. "Hollow the back and place your knees and feet fairly wide apart. Breathe through your mouth, bear down against the instrument, and tell me at once if you begin to feel pain." It is usually possible to find an artistic patient who will make a drawing of the position from the side which will help other patients at their first sigmoidoscopy.

Preparation of sigmoidoscope.—Between cases, the tube and obturator are cleaned, and boiled for 5 min. They should be used warm and lubricated.

Passage of sigmoidoscope.—After the first 2 in., aim for a point 1 in. deep to the left posterior inferior iliac spine. Do not attempt to pass the tube-cum-obturator beyond the 4-in. mark, and never continue insertion with obturator if pain results, but pass over at once to visual control, whereby the tube can be guided through the lumen so as not to traumatise the mucosa. Care rather than skill is required.

In general, it is best when passing the tube *up* the bowel to concentrate on correct manipulation, and when withdrawing it *down* the bowel to carry out the detailed study of the mucosa. Cases in which fæces or enema fluid obstruct the view should be deferred to another day.

No useful purpose is served by passing the tube to its limit if sufficient pathological evidence has already been found at lower levels.

Spasm should never be overcome by instrumental pressure; it nearly always passes off if one waits for a few seconds. Air injection is very seldom helpful.

Observation of lesions.—Little skill is required for the gross lesions, but the finer pathological changes, particularly the pin-point craters, call for careful technique. For these it is essential to use the stroking method, whereby the mucosa is examined by oblique illumination. This is achieved by gently tensing the bowel wall with the lip of the tube. The tube is held a little sideways against the area of mucosa under inspection, and so manipulated by slight change of angle and slight withdrawal that the mucosa slowly slips away under oblique illumination, passing in review as it goes.

After sigmoidoscopy, the patient should as a rule be informed of the result, since documentary evidence often becomes mislaid or unavailable, and any knowledge of the previous state of the bowel at future sigmoidoscopies is of great value.

One of the greatest advantages of the simple technique described is that it enables twenty or more sigmoidoscopies to be done in a morning without throwing undue strain on the ward staff. In this connexion, it is essential to have an enema room adjacent to the ward, where all preparations and therapeutic washouts and enemas can be conveniently given. Even retention enemas can best be given here, since almost all patients can walk a few yards thereafter without undue discomfort. This gives a great saving of labour for the ward staff.

The most careful supervision is necessary in the enema room to ensure prevention of cross-infection.

SUMMARY

The value of sigmoidoscopy in amœbic dysentery is discussed.

The normal mucosa and the different types of amœbic lesions are described.

The commonest amœbic lesion is the pin-point crater, usually seen 3–6 in. from the anus.

The technique of sigmoidoscopy, including the preparation of the patient, is described.

PENICILLIN IN SKIN CONDITIONS IN THE ARMY

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PENICILLIN has been available in the British Liberation Army (BLA) for skin conditions on a wider scale than ever before in the British Army, and several thousands of cases have been treated with it. It is felt that this experience should be recorded, even though it has been difficult under active service conditions to obtain well-controlled series of cases. In the early days penicillin was restricted to conditions which were essentially infections—e.g., impetigo, ecthyma, folliculitis, and possibly sycosis. Later, when there was more penicillin, it was used to deal with the infective element in septic eczema, seborrhœic dermatitis, sulphonamide dermatitis, &c., and parenterally for boils, carbuncles, &c.

TECHNIQUE

Penicillin spray, as originally suggested by Taylor and Hughes (1944), has been used in most cases. The simplicity of this treatment is one of its greatest assets, especially when large numbers of patients are being handled. The patients were usually sprayed three times a day with an ordinary throat-spray; more frequent sprayings have been tried, but they did not seem to produce any better results. Major P. H. Taylor, working in a camp reception station, treated a number of outpatients twice daily with spraying; the results were good but not so good as in men admitted to hospital and treated three times a day.

A solution of 200–500 units per c.cm. has been used. With a strength of less than 200 units per c.cm. the failure-rate increases, but no advantage seems to be gained by increasing the strength above 500 units per c.cm. The use of too strong a solution may even lead to sensitisation or at least irritation. Michie and Bailie (1945) reported such a case but would not assign a definite cause. The solution is easily prepared, even in forward units, by dropping a tablet of penicillin (5000–10,000 units) into 25 c.cm. of sterile water; this small quantity is rapidly used up, so there is little danger of its becoming inactivated. For skin departments in hospitals the solution is prepared daily in the laboratory.

Penicillin emulsion has also been used, made up with 30% 'Lanette wax SX' in water and containing 200–500 units per gramme. It is effective in the same types of conditions as the spray but is particularly useful in infected weeping areas which need a dressing. Occasionally, even in a simple impetigo, the emulsion may produce folliculitis; this is due to the base rather than the penicillin and occurs more often if there is any soft paraffin mixed with it.

To estimate the utility of penicillin emulsion for outpatients, Taylor and Hughes (1945) tested some which had been handled just as a patient would do—i.e., it was carried in a box in the pocket, and each day it was opened and a non-sterile finger put into it. They found that after a fortnight the potency of the penicillin had only been

reduced by 30%. This confirms previous work of Hughes who showed that modern samples of penicillin deteriorated more slowly, both in solution and in emulsion, than did older ones.

We have used penicillin emulsion successfully in out-patients in suitable cases, and this will probably be the method of choice in civilian life; but in the Army, where a soldier with any degree of skin infection is admitted to hospital, spraying is more convenient.

Parenteral penicillin.—Penicillin has only recently been used parenterally in skin conditions, hence it is difficult to assess its results. It has been useful in carbuncles, severe or recurrent boils, severe streptococcal infections round the ear, &c. The usual course has been 40,000 units followed by 20,000 units at three-hour intervals; up to about 500,000 units. Two cases of Rosenbach's erysipeloid successfully treated with penicillin given intramuscularly have been recorded by Hodgson (1945).

IMPETIGO

The number of cases of impetigo in BLA runs into thousands. The results obtained with penicillin have been better than we have seen with any other form of treatment. It might be objected that the soldiers in this army were a selected group and likely to respond well to any form of treatment once they had been admitted to hospital. This may be partly true, but it is not the whole story. In the early days of the invasion one saw many cases responding slowly to treatment in hospitals using the old methods, when these men were transferred to a hospital where penicillin was used they were cleared rapidly. Later, when all hospitals had been instructed in the use of penicillin, the quicker turnover was noted by all.

Treatment.—On admission the crusts should be cleaned off and the hair cut short over any scalp lesions before starting the spraying; thereafter the crusts are left untouched, but it is important that the patient should shave each day. At first, patients were discharged directly the crusts dropped off, usually after about 7 days, but a considerable number relapsed on returning to their units. This was largely prevented when the men were retained for a further 48 hours after the lesions had dried up and a mild antiseptic used, such as 2% ammoniated mercury in Lassar's paste or lotio cupro-zincica (*NWF*). It seems probable, though this has not been investigated bacteriologically by us, that penicillin does not destroy all the organisms, and that, once its influence has been removed, the survivors can again flourish, provided the soil is suitable.

The improvement with penicillin is usually striking; if a patient is not almost clear in 5 days, it is probable that he will not be cured by penicillin. There is evidence to show that penicillin fast strains may be produced if penicillin is used for more than about a week; if, therefore, a patient is not clear in that time, the treatment should be changed.

The conjunctivitis which is sometimes associated with impetigo also does well with penicillin either sprayed directly at the eye or smeared on the eyelids as the emulsion. In either case the danger of sensitisation from 'Albucid' or from boracic lotion, &c., is avoided.

TABLE I.—COMPARISON OF TREATMENTS OF IMPETIGO

Series	Cases	Failures	Average time of cure (days)	Treatment
F.F.H. (BLA)	141	9	8.5	Penicillin spray
G.A.H. (BLA)	63	4	8.8	
Total	204	13 (6.4%)	8.6	—
F.F.H. (UK)	100		13.7	5% sulphathiazole
Various (UK)	6000 +	11%	11.3	Microcrystalline sulphathiazole

Results.—A series of cases of impetigo was treated with penicillin spray followed by a day or two's treatment with a mild antiseptic. These were unselected cases, many very severe, but those showing such complications as otitis media, seborrhoeic or sulphonamide dermatitis were excluded. A man was not described as cured till he was written up for discharge with his skin apparently normal. No large control series is available in BLA, but the results of 100 similar cases treated with 5% sulphathiazole emulsion in England are recorded (table I); we have also given the figures of a very large series treated with microcrystalline sulphathiazole, the most effective form of treatment before penicillin was used. The results from other dermatologists in BLA were almost identical. Penicillin spray does therefore appear to be significantly better than sulphathiazole.

Causes of failure.—Bacteriological investigations have not been carried out on many of these cases, but it is probable that in some we have been dealing with organisms which were, or became, penicillin resistant. In an attempt to deal with such organisms a mixture of penicillin (600 units per c.c.m.) and 'Merthiolate' (1/1000) was used, after Major Hughes had shown that penicillin was stable in such a solution.

TABLE II.—IMPETIGO TREATED WITH PENICILLIN AND MERTHIOLATE

Series	Cases	Failures	Average days for cure
F.F.H.	31	3	7.4
G.A.H.	54	7	6.7
Total	85	10 (12%)	6.9

The results (table II) do not show any fewer failures than with penicillin alone. It is probable that the main cause of failure is not the penicillin resistance of the organism but the make-up of the patient. Many of the patients who fail to clear with penicillin also resist other treatments; they have often a history of previous attacks and are apt to relapse even when apparently cured. The lesions often affect the so-called seborrhoeic sites—e.g., the eyebrows, ears, scalp, &c., and there may be folliculitis of the beard area. We are convinced that the seborrhoeic background plays a very important part in the development, course, and prognosis of impetigo and impetigo like lesions.

ECTHYMA

Ecthyma occurs much more often in the Army than in civil life. It affects chiefly the legs, sometimes also the arms, and appears as little crusted ulcers which ooze pus from under the crust. When treated with gentian violet, &c., the ulcers will apparently heal over, but in a few days they break down again. In our experience ecthyma has been a difficult condition to cure consistently even in hospital, though some cases clear quickly with any treatment once the patients are in bed. We treat our cases by washing the legs daily with soap and water, removing any large crusts, and spraying three times a day with penicillin; the legs are left bare under a cradle, unless there is a lot of discharge. After about 6 days the lesions are clean and healing, and they are then treated with 2% ammoniated mercury in Lassar's paste or cod liver-oil ointment. The results were as follows:

Total no. of cases	45
Evacuated in an emergency (7th and 11th days)	2
Average days for cure (43 cases)	12.3
Average days on penicillin	6.1

The average time in hospital for ecthyma in the UK in pre-penicillin days was 30.1 days. We are voicing the general opinion of dermatologists in BLA when we say that we have never seen cases respond so quickly and so consistently to any other form of treatment.

SYCOSIS BARBÆ

Sycosis barbæ initially responds well to penicillin, but one can only speak of a cure when the patient remains permanently clear, and we have been unable to follow up our cases. Nevertheless one is often told by patients after a few days' treatment that they are already better than they have been for months or even years.

Treatment.—The penicillin is sprayed on for about 7–10 days—rather longer for sycosis than for impetigo. At the end of this time there is usually a well marked improvement and the treatment is changed to 'Quinolor compound ointment' or lotio cupro-zincica. To prevent relapses the patient is told to continue this application for a month. Some patients have been given penicillin

emulsion on discharge, or if they have later shown a tendency to relapse, and the condition has been kept under control Recently we have been using the emulsion more often in the initial treatment with good results.

Nasal infection is often present in chronic sycosis; in an attempt to deal with this, parenteral penicillin has been used a few times, but the results do not seem to be any better than with local penicillin alone. It is probable that an underlying seborrhœic state is an important factor in the resistance of both the sycosis and the sinusitis

Results.—The following results were obtained in 27 cases admitted to one hospital from October, 1944, to March, 1945 All had typical chronic sycosis of at least 3 months' duration, and some of many years. All patients discharged to duty were free from pustulation, with the skin apparently normal though sometimes a little red Most patients had been treated before by various methods with little permanent effect On admission they were treated with penicillin spray for about a week, followed by quinolor compound ointment, lotio cupro-zincica, or 5% sulphathiazole emulsion. The results were as follows

Total no of cases	27
Evacuated to UK	2
Transferred elsewhere for ENT treatment	3
Transferred elsewhere in an emergency	3
Returned to unit	19
Average days for cure (19 cases)	15 4
Average days on penicillin	7 6

The average time of stay in hospital of patients with sycosis in the UK in 1943 was 36 2 days.

Although we have no control series, the immediate results are superior to any we have previously obtained in this notoriously difficult condition; actually many soldiers provided their own control in the length of time they had been unsuccessfully on other treatments. It is certain, however, that many of these cases will relapse, and one cannot say whether they will always continue to respond to penicillin, the few relapses we have seen were easily controlled by more treatment

BOILS

With boils it is impossible to give statistical evidence of any value, and we merely state our impressions. Penicillin spray does not do any good in real boils, though it does help in the superficial folliculitis which one often sees round a boil, or where elastic p aster has been applied, or mixed with impetigo It is possible that penicillin emulsion may help occasionally in boils.

Parenteral penicillin will often cut short an attack of boils and is particularly useful in severe multiple boils of the back of the neck or in the axilla We have tried it also, often with apparent success, in recurrent boils, one must not, however, neglect adjuvant measures such as the avoidance of friction from rough or dirty clothes, and the frequent sterilisation of the skin by washing with soap and water Our usual course of penicillin has been about 500,000 units

In carbuncles the results are sometimes dramatic and the pain is greatly relieved in 24 hours, the carbuncle still takes a considerable time to heal though no longer painful We have occasionally seen carbuncles recur only a week or so after courses of 1,000,000 or even 2,000,000 units.

INFECTED ECZEMA, SEBORRHŒIC DERMATITIS, AND OTHER CONDITIONS

Penicillin is of definite value in the treatment of infected eczema and seborrhœic dermatitis if used judiciously, but it can only clear up the infective element and has no action on the underlying eczema or other condition. One great advantage of penicillin is that it is hardly ever irritating, and so there is little danger of aggravating an already inflamed skin, as may happen with other antiseptics Many of these cases show a remarkable improvement during the first 4 or 5 days, more sometimes than one would have anticipated, suggesting that the infection is playing a large part in keeping the dermatitis going. However, after this the condi ion seems to come to a standstill, and at this stage a change of treatment to some bland application is indicated. This point is emphasised because some people have maintained that penicillin dries the skin, whereas in fact it has cleared away an infection and revealed an underlying dermatitis

This treatment has been useful in cases of acute sulphonamide dermatitis complicating impetigo or seborrhœic dermatitis (we have had over 500 cases of sulphonamide dermatitis in BLA) Usually the skin has been sprayed three times a day and left exposed to the air, but, when there has been much discharge, a dressing of lint thickly covered with penicillin emulsion has been used instead

In otitis externa penicillin has on the whole been disappointing; it is best applied as an emulsion on a wick of gauze, but many cases fail to respond either owing to insensitive organisms or an underlying seborrhœa

We have sometimes used parenteral penicillin in severely infected pompholyx with lymphangitis and adenitis, especially if the patient is sensitive to sulphonamides. It has been particularly useful in cases of badly infected seborrhœic dermatitis with tense swollen ears or intractable oozing and crusting of the scalp Local treatment has consisted chiefly of a good washing of the scalp with soap and water, removal of the hair, and application of some bland cream.

Cutaneous diphtheria—We have successfully treated a few cases of cutaneous diphtheria with local penicillin, but antitoxin has been given at the same time. The treatment has been the same as for ecthyma, and the sores have rapidly become sterile

CONCLUSIONS

Penicillin, when properly used, is of great value in dermatology, particularly in impetigo, ecthyma, sycosis, and infected eczema It rapidly eliminates the infection with almost complete absence of irritation and hence is greatly to be preferred to the sulphonamides. Used as a spray it is a simple and rapid treatment and practically eradicates the danger of cross-infection in the treatment room. For outpatients the emulsion is more suitable. Almost all the benefit from penicillin is obtained within 7 days; if there is no decided improvement by then, further continuation of this treatment is useless Failure may be due to resistant organisms but is often attributable to the patient's constitution, especially the presence of an underlying seborrhœic tendency.

We wish to thank the dermatologists of BLA who have all made some contribution to the use of penicillin in dermatology, Major K E A Hughes for advice and help on the bacteriological aspect, and Major-General E Phillips, DMS, 21 Army Group, for permission to publish this article

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THROUGH-AND-THROUGH BULLET WOUNDS OF THE MEDIASTINUM

WITH RECOVERY

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IT seems rare for cases of through-and-through bullet wounds of the mediastinum to survive evacuation from the forward area Nicholson and Scadding (1944) describe one such case, out of 201 penetrating wounds of the chest, which made a rapid and uninterrupted recovery D'Abreu, Litchfield, and Hodson (1944) describe 12 with retained metallic foreign bodies in the pericardium, endocardium, or mediastinum, out of 264 severe chest injuries seen 2–50 days after injury.

The following 3 cases of through-and-through bullet wounds of the mediastinum occurred in a series of 11 penetrating wounds of the chest Only 1 of the 11 died; not o e hæmothorax became infected, and all except one (case 3) were seen within a few hours of injury.

CASE 1, aged 22; wounded at 3 PM and admitted to hospital at 7 20 PM on Dec 14, 1944 He had a through and-through bullet wound, the entry being in the 5th left interspace in the mid clavicular line, and the exit in the 7th right interspace in the mid-axillary line. He was shocked and too

ill to be disturbed even for us to examine his back or to take his blood pressure An intravenous drip serum was discontinued after 500 c cm had been given. On the 2nd day the blood pressure was 90/50 mm Hg and the heart sounds muffled On the 7th day a chest radiogram showed a right hæmothorax, a hæmopericardium and a shadow in the left middle zone—probably unabsorbed blood in the lung tissue—along the path of the bullet (fig 1) The blood pressure was 80/50 mm Hg and the patient dyspnœic The pericardium was needled, but only a small quantity of partially clotted blood was obtained, and it was decided not to intervene further at this stage

On the 12th day the patient got out of bed unobserved On the 25th day he was evacuated He then walked well A radiogram on Jan 5 showed the heart shadow to be normal and the lung fields clear, except for some "peaking" of the right diaphragm (fig 2)

CASE 2, aged 22; admitted at 5 30 P M on Dec. 12, 1944 He had been shot through the chest in the forenoon by a sniper; owing to further sniping he could not be picked up immediately, and while he was being carried in, one of the bearers was killed and the patient was wounded a second time, now in the right thigh He had two through-and through bullet wounds one with entry in the 1st left interspace immediately lateral to the sternal border and with exit in the 3rd right interspace in the posterior axillary line, the second with entry on the outer side of the right thigh, and exit over the pubis 2 in to the right of the midline His general condition was so grave that he was not even examined further A blood transfusion was discontinued after 150 c cm. had been given because he had a rigor He seemed likely to die at any time during the first 48 hours, but after that time steadily improved, and when then examined was found to have a right hæmothorax On the 10th day the signs of right hæmopneumothorax were confirmed radiologically (fig. 3) The chest was needled on the 11th day 30 oz. of altered fluid blood being aspirated; this was sterile Aspiration was repeated on the 14th day, 15 oz being removed again sterile On the 17th day he was evacuated. His general condition then was satisfactory, the wounds in the thigh and in the chest wall had healed by first intention but the hæmopneumothorax had not resolved Two months after injury, on Feb 21 1945, it was reported from a base hospital that this man's right lung had expanded fully after one subsequent aspiration he was then ambulatory, awaiting transfer to a convalescent depot

CASE 3, aged 27; admitted at 3 P M on Dec 30 1944 He had been wounded by a bullet 7 days before, and had been transported to the hospital ship on a motor launch It was stated that he had had hæmoptysis, and that he had been given sulphonamides by the mouth He had a bullet wound with entry in the 8th right interspace in the anterior axillary line; the bullet was palpable beneath the skin 1 in below the junction of the middle and inner thirds of the left clavicle His general condition was good; there was a large right hæmothorax (fig 4) which was aspirated; cultures sterile Nine days after admission having steadily improved he was evacuated

These cases were treated in the medical wards on conservative lines, and we tried to concentrate on the patient as a whole rather than on his injuries Intravenous infusions were purposely small, and intrathoracic hæmorrhages were not aspirated for at least a week, because it was feared that in these cases with possible trauma to mediastinal vessels any measures tending to raise the blood pressure, or to lower the intrathoracic pressure, might prolong the bleeding or cause it to recur

During the first 48 hours the patients were not moved, being left in bed in the clothes in which they arrived They were given morphine in sufficient quantities to make them apathetic for the whole of this period, and a nurse was available at all times to persuade them to take fluids by mouth whenever they roused Of these they took liberally, preferring cold water or warm sweet tea

Penicillin was given intramuscularly, 20,000 Oxford units 3 hourly, from 12 hours after admission until it was considered that repair was well advanced Whenever a hæmothorax was aspirated 40,000 units of penicillin in 20 c.cm of saline was inserted into the pleural cavity

Circumstances which possibly predisposed to survival in these patients were that they were young, they did not appear to be over awed, either by their repeated hæmoptyses or by the serious nature of their injuries, and they were admitted to hospital early Fighting took place in a port and the seriously injured were transported directly to the hospital ship, lying offshore: in consequence, there was not the frequent changes in medical and nursing staff usually associated with transportation, and from the beginning they were under the full time care of a single medical officer In the same ward over the same period were 8 other men with penetrating bullet wounds of the chest, only 1 died

SUMMARY

Three cases are reported of through-and through bullet wounds of the mediastinum which occurred in a series of eleven penetrating wounds of the chest

All three developed hæmothorax, and one developed hæmopericardium in addition

Two were treated by repeated aspiration and injection of penicillin into the pleural cavity, all had prophylactic intramuscular penicillin

In the third, the intrathoracic effusions of blood resolved spontaneously without serious complications All three recovered

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Fig 1—Case 1, Dec. 21 1944.
Fig 3—Case 2, Dec. 22 1944.

Fig 2—Case 1 Jan. 5 1945.
Fig 4—Case 3, Jan. 5 1945.

Reviews of Books

Essays on Growth and Form

Presented to D'Arcy Wentworth Thompson
Editors W E. LE GROS CLARK, FRCS, FRS, P B MEDAWAR. (Oxford University Press Pp 408 21*s*)

THIS fine book shows the remarkable progress made since D'Arcy Thompson set the snowball rolling with *Growth and Form* W E Le Gros Clark discusses the thesis that the sulcal pattern of the brain is largely determined by extrinsic mechanical factors—such as stresses set up during development, and the shape of the skull V B Wigglesworth follows with a study of the growth of the blood-sucking bug Rhodnius, which leads him to conclude that each living organism is a giant molecule, divided (in multicellular animals) into cells for purposes of "administration" Having thus released us from the incubus of the cell theory, he goes on to suggest that the cells, influenced by genes and hormones, care for and maintain that fragment which they carry of the chemical continuum which is the organism The cells therefore do not coöperate to mould body form, but are only the agents of the "pervading web which is the organism itself" As D'Arcy Thompson wrote, they "enter like a froth into its fabric"

J Z Young contributes an important essay on the shape of the nerve fibre, and J H. Woodger reminds us to think of organisms as time-extended and time-differentiated by using the terms "time-slices" (momentary states) and "time-stretches" (the five epochs into which he divides the life of an organism). Examining the theory of transformations, he suggests that we need a theory of cytoplasmic organisation, as well as such theories of the zygote structure as that of the gene, which was devised to explain the distribution of properties in mendelian ratios rather than embryological data He thinks that D'Arcy Thompson's methods can be applied only during later phases of development, when changes of shape and size are primarily involved, and that taxonomy and morphology would be transformed by explaining early development in terms of the production and mutual interaction of parts, with the inclusion of time relations, for in this way a classification of adults would be replaced by a classification of zygote types Among other essays are those by E. C R Reeve and Julian Huxley on allometric growth, by O W. Richards and A. J. Kavanagh on the analysis of growing form, and by P. B Medawar on size and shape as functions of age W T. Astbury, in discussing the giant molecules of the proteins, polysaccharides, and nucleic acids, seeks to bring physics and biology closer together in the study of the structure of matter, and E N Willmer, considering growth and form in tissue cultures, suggests a scheme of cell lineage which illustrates how the growth and form of tissue culture cells may be related to the embryological and phylogenetic origin of these cells J F. Danielli, reflecting on problems of surface tension in the simpler cells, concludes that the main obstacles to progress in the study of cell form is the lack of suitably trained men with a sufficiently wide scientific education. Many will agree with him that much scientific thought is unconscious, and that its quality therefore depends upon the educational background of the worker—who should be given the opportunity to make this background adequate

Advances in Enzymology and Related Subjects of Biochemistry

Vol V Editors F F. NORD, C H WERKMAN (Interscience Publishers Pp 268 $5 50)

THE title of this series suggests that the contents are likely to be stiff reading for the ordinary medical man: and so they are, being written by experts, responsible for part of the original work they describe, for fellow scientists working in the same field Of the eight articles two are by workers in this country and the remainder by Americans They range from the physical and chemical properties of tomato bushy stunt virus and the strains of tobacco mosaic virus to recent progress in the biochemistry of fusaria An article on coagulation of the blood by Chargaff, though strictly biochemical, is of general importance, and there are many points of medical interest Blaschko's article on the amino-acid decarboxylases of mammalian tissue; a more critical opinion about the normal and abnormal excretions of histidine and histamine during pregnancy would have been welcome, however The article on pyruvic metabolism demonstrates conclusively the important part played by this compound in intermediary metabolism. Direct fermentation of disaccharides are discussed, and there is a short paper on the enzyme reactions of sulphur compounds. The editors and the authors are to be congratulated on producing this international journal under difficult conditions

Diseases of the Nervous System

In Infancy, Childhood, and Adolescence (2nd ed.) F R FORD, MD, associate professor of neurology, Johns Hopkins University (Baillière Pp 1143 47*s*)

THE neurology of childhood, as Dr Ford pointed out in the preface to his first edition, belongs both to the neurologist and the pædiatrician, but has not been cultivated intensively by either It includes a vast number of congenital abnormalities and hereditary diseases, infective conditions peculiar to childhood, and the whole of the neurology of mental defect. In addition, except for the degenerative disorders of later life, children are subject to most of the nervous diseases occurring in adults. Dr Ford's encyclopædic work fills a gap in neurology, and the second edition maintains the high standard of the first. It is difficult to find even trifling omissions

Fundamentals of Electrocardiographic Interpretation

(2nd ed.) J BAILEY CARTER, MD, FACP. (Charles C Thomas Pp 406 $6)

THE new edition of this practical handbook has been thoroughly revised, and special attention has been given to the findings in coronary disease. Written primarily for the physician who has no detailed knowledge of the subject, it avoids controversial matter and gives straightforward description of the commoner electrocardiographic findings and their interpretation. Sufficient theory is included to clarify the underlying principles The extensive bibliography is selected from American and British sources Some of the 307 figures are so poorly reproduced—doubtless owing to war-time difficulties—that they cannot be accurately interpreted, but this will undoubtedly be remedied in future editions. Some are on too small a scale Clear reproduction is essential in atlases of electrocardiography such as this.

Arthritis and Allied Conditions

(3rd ed) BERNARD L COMROE, MD, FACP, senior ward physician and chief of arthritis clinic, Hospital of University of Pennsylvania. (Kimpton. Pp 1359 60*s*)

IN his third edition Dr Comroe has added new chapters on such subjects as penicillin, and rheumatic manifestations of tropical diseases, occupational therapy, and mistakes in the diagnosis and handling of patients with arthritis and allied conditions He has collected facts diligently; the specialist will find interesting new material on the disabling changes resembling sclerodactylia in the hands, and the palmar changes typical of Dupuytren's contracture which may follow myocardial infarction; and the general practitioner can learn much from the book. But it is disappointing that so much material was collected and so little of it investigated "There is too little speculation and too little use of the imagination," as Sir Robert Hutchison said in another context Dr. Comroe does not cater adequately for the needs of the student, the general practitioner, or specialist Methods of treatment which are either unconfirmed or already somewhat discredited—such as ACS serum or ertron—figure prominently in the text; Mester's test, which he holds to be grossly unreliable, has in several recent papers from South America been found accurate in over 97% of cases Nevertheless, this is the most comprehensive book on rheumatic disease in English, and Dr Comroe had already earned our thanks. The younger doctors are becoming increasingly interested in rheumatism, and many of them will use this book. May we hope that in the next edition, Dr. Comroe will omit some of the accumulated facts in favour of an exposition of principles and practice derived from his exceptional clinical experience?

THE LANCET

LONDON SATURDAY, OCTOBER 13, 1945

The Sanatorium Nurse

The MINISTER OF HEALTH has decided that Mantoux-negative nursing candidates should not be excluded from sanatoriums and chest hospitals or from the general wards of other hospitals[1] The reasons on which this decision is based are set out in a report on tuberculin testing from a special sub committee of his standing advisory committee on tuberculosis, and this has been circulated to the interested authorities Mr J E H ROBERTS, Dr JAMES WATT, and Dr J S WESTWATER composed the subcommittee, and they coöpted Dr MARG DANIELS, Dr P D'ARCY HART Dr MARGARET MACPHERSON, Dr FRANK RIDEHALGH, and Dr NORMAN F SMITH, while Dr HARLEY WILLIAMS acted as secretary

The report points out that no evidence relating to Great Britain exists to show the relative risk of developing tuberculosis for nurses working in various types of hospitals and in sanatoriums In our view, however, this absence of evidence, which is repeatedly invoked to excuse vagueness about the dangers or otherwise of sanatorium nursing, should now be recognised as a stumbling block to progress rather than a convenient piece of cover Though observations on nurses in general hospitals in this country have shown, as the report notes, that the Mantoux-negative nurse runs a greater risk of developing active tuberculosis than the Mantoux positive nurse, the subcommittee do not think it in the interests of either the nurse or the public to debar negative reactors from sanatorium nursing The most weighty argument in favour of this opinion is that, with increasing control of tuberculosis, Mantoux negative young women will become more numerous, and if they are prohibited from sanatorium nursing the pool from which such nurses can be drawn will become progressively smaller The subcommittee argue that it is to the advantage of these girls to admit them to tuberculosis nursing under expert supervision, since this will ensure early and adequate treatment if they become infected This is right enough, always provided the sanatoriums recognise the full weight of their responsibility and make no mistakes in discharging it. There is less justification for the statement "If it comes to be believed by the [nursing] profession, and the public that Mantoux-negative reactors run undue risks in sanatorium or hospital nursing as compared with other forms of employment the supply of these nurses will progressively diminish" The point at issue, surely, is not what "comes to be believed" but what is true If investigation shows that there is no undue risk, the sooner the figures are published the better, if in fact it shows the reverse, then we have been allowing negative reactors to undertake dangerous work without giving them accurate warning of the risk The sub committee are clearly not at ease about their decision, for they say—

> "We think, however, there may be some case for excluding Mantoux negative nurses from advanced pulmonary wards, although there is strong evidence to show that, even in the worst conditions, risks may be considerably curtailed through the using of masks and other simple personal precautions."

Here the "risks" are frankly admitted

The standard of care which the subcommittee recommend for the negative-reactor is thorough and high, including Mantoux tests every three months, X ray examination on entry to hospital and afterwards at twelve monthly or six monthly intervals, and monthly weighing The chest should be radiographed as soon as the test changes from negative to positive, and thereafter every three months for a year or longer, and in any case on the development of symptoms The health of these nurses should be under the care of a senior member of the medical staff, and records of examinations should be open to inspection by the Ministry The MINISTER, in his covering circular, endorses these recommendations fully, adding that they should apply also to domestic staff who are exposed to infection, and he advises that the careful standards of Mantoux testing laid down by the sub committee should be generally adopted In the best sanatoriums the high level of care advocated in the report has been achieved already[2], but some time must pass before such care becomes general In poorly run sanatoriums and small private nursing homes for the tuberculous, shortage of staff is often so acute that the health of the nurse—sometimes a girl as young as 15 or 16—is sacrificed to that of the patients Nor is the experience of nurses who take the infection reassuring on the whole the records of 80 such cases collected privately by Miss E D ANDREWS show that few had encountered that overriding concern for their welfare —physical or financial—in which the subcommittee seem to put their trust

If the welfare of the tuberculosis nurse is not considered on its own merits, expediency will naturally colour the findings The problem of staffing the sanatoriums is a part of the problem of staffing the hospitals as a whole

1 Circular 166/15 dated Sept 28

Wisdom from Rats

FOR some years, at the psychobiological laboratory of the Johns Hopkins Hospital in Baltimore, RICHTER and his colleagues have been making experiments which demonstrate the reliability of the rat's appetite as a guide to its dietary needs[3] Their latest observations[4] not only confirm this wisdom among rats, but also throw light on diabetes mellitus in man A group of rats had access to casein, dextrose, olive oil, five different mineral solutions, six different solutions of vitamin B components (thiamine, riboflavine nicotinic acid, pyridoxine, calcium pantothenate, and choline), cod liver oil, and tap water each in a separate container The rats selected large amounts of carbohydrate, moderate amounts of protein and minimal amounts of fat, and on this diet gained weight and remained in good health After a time they were all subjected to subtotal pancreatectomy, and immediately afterwards they chose to increase their intake of protein and of the various components of the vitamin B complex Some three weeks later there was a

2 Edwards J W, Dewman, A. C. *Lancet* 1945 i 1[illegible]
3 Richter C P *Harvey Lect* 1942-43 38 [illegible]
4 — Schmidt C H., Jr., Malone J D *Bull Johns Hopk Hosp* 1945 76 192

sharp reversal in their appetite for carbohydrate and fat, compared with that before operation, the average caloric intake of carbohydrate falling from 65 to 30%, while the fat intake rose from 15 to 39%, and the protein intake from 20 to 31% As long as they remained on this diet they maintained their weight and showed no definite symptoms of diabetes mellitus; but as soon as they were placed on a stock diet, with constituents in fixed amounts, they developed all the symptoms of diabetes—thirst, polyuria, increased appetite, loss of weight, loss of energy, and lenticular cataract Neither the addition of protein, nor of protein plus the various components of the vitamin-B complex, increased their activity or decreased their thirst, but the addition of protein with vitamin B and olive oil resulted in both an increase in activity and a fall in the intake of water

RICHTER'S view is that after pancreatectomy the rats cannot use carbohydrate, and therefore eat more of the stock diet in order to obtain calories from the fat, which they are able to use This is the explanation of diabetic hunger The greater intake of stock diet results, of necessity, in an increased intake of carbohydrate; and since this cannot be used, extra fluid is needed to enable the kidneys to excrete the excess remaining in the blood-stream; hence the polyuria and polydipsia Protein is lost after pancreatectomy, and the rats cannot get enough protein from the stock diet to replenish this loss, so they lose weight Activity is impaired because ingestion of large amounts of carbohydrate is enforced by the diet, while the intake of fat and protein—the only sources from which energy can be obtained—is inadequate On the diet they select for themselves the rats ingest small amounts of carbohydrate, thus avoiding a high blood-sugar, polyuria, and polydipsia The increased amounts of vitamin B taken allow them to make better use of carbohydrate and protein, and the greater intake of fat and protein eliminates the need for polyphagia Their activity is maintained by the fat

High-fat low-carbohydrate diets are no novelty in the treatment of human diabetes, having been widely used in the days before insulin More recently, MARKS and YOUNG [5] found that dogs rendered diabetic by injection of anterior pituitary extract lost most of their glycosuria and ketonuria when maintained on an almost exclusively fat diet Moreover, alloxan diabetes in rats can be kept under control by diets containing 80–90% of fat [6] There has been less agreement about protein requirements, but this may be, as RICHTER suggests, because high-protein diets have not necessarily been accompanied by a high intake of the vitamin-B complex, which seems to play an important part in protein metabolism What is good for rats may not be good for man, but a case seems to have been made out for investigating the effect on human diabetes of a diet rich in fat, protein, and vitamin B Moreover, RICHTER'S observations put a different complexion [7] on HIMSWORTH'S observation that diabetic patients, before diagnosis, instinctively select a high-fat diet; it now seems less likely that this high-fat intake predisposed to diabetes and more likely that it was instinctive therapy.

5 Marks, H. P., Young, F. G. *J Endocrinol* 1939, 1, 470
6 Burn, J. H., Lewis, T. H. C., Kelsey, F. D. *Brit med. J* 1944, ii, 752.
7 Himsworth, H. P. *Clin Sci* 1935, ii, 95

Background of Pollen Allergy

CHARLES BLACKLEY in his *Experimental Researches* on hay-fever (1873) laid the foundations of all subsequent work on pollen allergy Forty years or so later J FREEMAN and L NOON, armed with a knowledge of the modern technique of desensitisation, began to use the extracts which have proved so valuable in the treatment of pollinosis American workers about the same time revived BLACKLEY'S gravity method of exploring the pollen-content of the atmosphere and they have since published the results of several surveys based on this technique No such work was done in Britain, however, until late in 1941, when H A HYDE and D A. WILLIAMS began a daily census of atmospheric pollens caught on the roof of Llandough Hospital, Cardiff, which has been continued since without interruption A preliminary note of their results was published in January, 1943,[1] and a complete report for the year 1942 appeared in 1944 [2] This was the first survey of the kind in Europe and there was therefore no satisfactory handbook to the pollens likely to be encountered Hence the investigators had to begin by learning how to recognise the fifty-odd types of pollen with which they were confronted

They found that before the middle of March, and after the end of August, pollen was either absent from the air or was present in a concentration so low as to be unlikely to evoke an allergic response During the spring several tree pollens were at various times abundant enough to be responsible for so-called hay-fevers occurring before the end of May. Grass pollens were noted in very high concentrations from about June 1 until the third week in July The 1942 census showed that pollen fron plantain (plantago) and from sorrels and docks (rumex), both of which have been regarded as possible causes of allergic diseases in this country, were present continuously over some months, though not in quantities comparable with those of grass pollen Nettle (urtica) pollen was distinctly more plentiful, but its clinical significance is unknown The only pollen to appear on the Cardiff slides exclusively and in some quantity in late summer was that of the genus artemisia, which, with related pollens, is notoriously associated with late summer hay-fever in America One species (*A vulgaris*) sometimes dominates the vegetation of disturbed areas and may therefore deserve the attention of allergists in this country The incidence of each of the main types mentioned could be related to the local flora and local weather conditions In the aggregate grass pollens formed three-quarters of the total deposit during June and the first three weeks of July, but their concentration varied greatly from day to day and presumably the risk of their causing symptoms varied correspondingly It was evident that it would be worth while to attempt to analyse these changes, and a closer study of diurnal variation in the incidence of grass pollen was therefore made in 1943 and 1944 [3] Slides were exposed continuously and changed two-hourly at stations sited in the middle of grassy vegetation and on a building at a short distance therefrom, while at the same time a close watch was kept on the progress of flowering of

1 Hyde, H. A., Williams, D. A. *Nature, Lond* 1943, 151, 82
2 *New Phytol* 1944, 43, 19
3 *Ibid*, 1945, 44, 83

the principal grasses and on changes in the weather It was found that on fine sunny days these grasses flowered slightly in the morning but profusely in the afternoon the liberation of pollen was crowded into the short period following the mass flowering, and the concentration of pollen in the neighbouring air rose and fell correspondingly without any perceptible lag On dull days flowering remained largely in abeyance and local pollen concentration remained low

Certain conclusions important to allergists may be drawn from the results of HYDE and WILLIAMS's experiments In the first place, the pollen concentration near grassy vegetation is seen to vary enormously according to the time of day and the state of the weather During the midnight hours, even in fine weather at the height of the grass season, it may be very low indeed On the other hand, at certain times, depending on the flowering habits of the dominant grasses, the pollen concentration rises to previously unsuspected levels At Llandough, just after midsummer on fine sunny days, maximum values are attained in the late afternoon, on dull days no such rise takes place In other localities, where the principal grasses flower in the early morning, the maximum pollen incidence is likely to be at that time of day, provided the air is not too still, though the intensity of flowering may be affected by the amount of sunshine received on the previous day Secondly, the investigations have furnished information about the value of daily slides as a means of estimating pollen concentration American workers generally have used 24-hour gravity slides, and though these give a general indication of pollen incidence the figures obtained with them tell us nothing about changes during the day Daily counts of gravity slides have sometimes been used in computing atmospheric pollen concentration in grains per unit volume, assuming the grains to be free to fall vertically in accordance with Stokes's law But the resulting figure is at best only an average for the whole 24 hour period, and the new experiments show that so far as grasses are concerned it can have no real meaning

It is evident that HYDE and WILLIAMS are exploring with remarkable thoroughness the botanical background of pollen allergy Already they have shown that observation of the principal types and quantities of pollen in the air is essential to the proper study of hay fever and related conditions Clinical medicine is not the only branch of science which should benefit from such fundamental researches the repercussions will be felt in plant biology, geology, meteorology, and elsewhere Palynology, to use the new term which they have coined for the study of pollen and other plant spores, is a science with a future[4] From the medical standpoint such research may be regarded as an essay in human ecology—an inquiry into one special aspect of man's environment—and it is being carried out, quite appropriately, by a museum botanist (Mr HYDE is keeper of the department of botany at the National Museum of Wales) and a doctor (Dr WILLIAMS is deputy medical superintendent and physician at Llandough Hospital) Other such combined background studies might also be fruitful

4 Editorial Nature Lond 1945 155 261
5 Hyde H A Museums J 1944 44 115

Annotations

THE GOVERNMENT SCIENTIST

THE white paper on the Scientific Civil Service[1] deals with reorganisation and recruitment of scientists during the reconstruction period At the outset the Government acknowledges the nation's debt to the scientists in its employ "their contribution may have altered the whole course of the war, and has certainly shortened its duration" The Government "is resolved that the conditions of service for scientists working in State service shall be such as to attract scientifically qualified men and women of high calibre" This is a worthy acknowledgment and resolution Unhappily the white paper falls far short of it in performance

Though there are some improvements in salary, particularly for juniors and the highest of the seniors, a number of intermediate grades have actually had their ranges reduced, and in almost no case have the levels approached those paid to administrative civil servants The white paper gravely states that "a scale structure identical with the administrative class would not meet the requirements of scientific organisations This sounds suspiciously like Treasury eyewash, with which civil service negotiators are only too familiar It appears, indeed, that the administrators still intend to keep the technicians in their place Yet, as the *Manchester Guardian* remarks, "the notion that the administrator is inherently superior to all professional specialists is in consistent with the modern expansion of governmental functions"[2]

Another retrogressive feature of the white paper is the introduction of a lower rate of pay for scientists working in the provinces It is hard to see why the Government should think that a scientist in Oxford or Cambridge can, or should exist on a salary less than obtains in London

SILENT FILM IN MEDICAL TEACHING

THERE seems to be a tacit assumption that medical teaching films will be sound films This may be because for the man in the two and fourpenny seat, and also, if he is unlucky for the film director he meets at his club all professionally made films are sound films today It is also because many of our best recent films are sponsored whether by the British Council or by commercial bodies partly for prestige reasons and so have to be sound films if they are not to look out of date Experienced teachers and visual-education experts are raising their voices to remind us of the silent film because they know that for some purposes it is better This is apart from the higher cost of sound films and of sound projectors, the shorter life of sound films the greater difficulty of projection with sound the larger numbers of silent projectors, and the fact that silent films are more easily adapted for distribution abroad With a silent film the student can more easily think on his own lines than against a spoken commentary; he can learn more actively This is important for the film suffers from the defect of being a group method of teaching (though in practice the skilful use of films is followed by increased individual reading) For the teacher the silent film makes it possible for him to comment in a way adapted to his class and to vary his comments according to whether it is the first, second or revision projection He can also more easily fit a silent film into his present plan of teaching and as Meredith[3] has pointed out unless this is so, the introduction of the film as a new teaching weapon will fail

The question is not one of sound films *versus* silent films; we must decide the place of each type and whether for a particular film a commentary is helpful The short

1 The Scientific Civil Service Cmd. 6579 London HM. Stationery Office 3d
2 Sept 22 1945
3 Meredith G I Documentary News Letter 1944 No 1

"illustration" film—e g, of the facies in Bell's palsy—to be used in the course of a lecture is usually better silent The more complex "lesson" film can more usefully have a commentary, but even here silent films have a place, perhaps especially in those made to introduce the preclinical student to his work among patients For advanced subjects expounded by authorities in each field, and for "background" films, such as those on housing and nutrition relative to social medicine, sound is necessary

How does the case of making the two types compare? Silent films are usually, though not always, quicker and less expensive to make Useful films have been made by amateurs for the cost of the film stock, but the cost of a good ten-minute silent "lesson" film would be around £250 if all the time spent on it were paid for, while a sound-film of similar length would reasonably cost £1000 Money can easily be wasted in making silent films, but with a good team the lack of sound, and consequent emphasis on the visual approach, is often a challenge accepted with good results

As regards films for teaching medicine, "the urgent need is to enlarge the field of experience (in the use of films and other visual aids) as quickly as possible," to quote an editorial[4] on the Future of the Educational Film which should be read by everyone interested in medical education If the silent film takes less time and money (though as much thought) and for certain purposes is the ideal type, a way of attacking the present shortage of medical films is clear Let a small group of medical teachers and visual-education experts discuss the teaching of, say, neurology The various visual aids (diagrams, models, pathological specimens and sections, lantern slides, film-strips, silent and sound films) required would be decided in outline Some of these are already available and in use, for medical education has a good visual tradition Of those still unmade, some, such as diagram films on the anatomy of the CNS, or lesson sound-films on the dysarthrias, may take a long time to complete, but if production of the film-strips and silent films is started now, a notable supply could be assured in a short time and valuable experience gained For illustration films of the nervous disorders, a basic schedule could be worked out and a number of units employed simultaneously If none of the present commercial units can spare time, then semi-official medical film units, comparable to the present Service film units and staffed with personnel released from them, might be set up, though in the long run it would be unwise for such units to do only technical medical films These are details, the essential thing is that the important place of silent films in medical education should not be forgotten and that advantage should be taken without delay of their greater speed and lower cost of production to "enlarge the field of experience" of teaching medicine by films

RESTLESS LEGS

"A COMMON but practically unknown disease," described by Ekhom[5] under the title of "restless legs," occurs in two forms—one paræsthetic and one painful—and Ekhom's monograph is based on 154 cases of the former (34 severe) and 15 of the latter In the first form the presenting symptom is paræsthesia of a peculiarly disquieting type often described by the victim as 'crawling These sensations are usually felt between the knee and the ankle although sometimes in the thigh, and are accompanied by a feeling of weakness They are so persistent and disagreeable that they compel the patient to keep moving his legs or walking about to gain relief The symptoms appear only when the patient has been resting, particularly soon after he has gone to bed In mild cases they pass off in a few minutes, but they may persist for hours, interfering with sleep. Spontaneous remissions are common In the painful form the pain, which may or may not be accompanied by paræsthesia, has the same distribution in the legs and may be very protracted In neither group can any clinical signs be detected. The commoner, paræsthetic, form usually responds to carbachol in doses of 2 mg four to six times daily by mouth The intermittency of the symptoms differentiates the condition from polyneuritis or subacute combined degeneration of the cord, while the absence of involvement of the fingers excludes acroparæsthesia

A similar condition has been described by Allison[6] under the characteristically transatlantic title of "leg jitters" This consists of a curious unlocalised restlessness in one or both legs which is said to be distinctly unpleasant It usually comes on when the legs get warm in bed, and is relieved by getting up and walking about Immediate relief is obtained by chewing gr 1/100 of nitroglycerin, and for this reason it is thought to be vascular in origin Ekhom places the "restless legs" he describes in the category of those "chronic diseases with exclusively or mainly subjective symptoms which embitter but do not endanger the patient's life," but he disputes the inevitable suggestion that they are neurotic in origin Many clinicians will welcome this refusal to call a condition a neurosis simply because no organic lesion can be demonstrated

THE NURSING CRISIS

THAT shortage of nurses is already lowering standards of care given to patients was the gist of the message which four nurses carried in person to the Minister of Health not long ago Their visit to him was a sign of the growing concern at this decline in standards—a decline which must continue unless we can fill the ranks of a profession which should be among the most natural and rewarding for women.

So far, public attention has been largely directed towards recruitment of nurses, but the real problem is not so much how to attract candidates as how to keep them when we have got them The annual numbers of entrants to the profession have risen steadily since registration was introduced, and people with experience of recruitment say that a campaign will always bring in fair numbers of candidates; but a wastage of nearly 60% during the training years argues serious defects in the conditions under which the work is done In an industry, such a high loss of personnel would be the signal for a drastic revision of policy The many drawbacks to the nurse's life have been laboured enough in these columns and elsewhere, but to take a representative point mentioned this week in a letter from Dr S W Swindells, no industry in this country would attempt, as the hospitals do, to cover a 24-hour day in two shifts Nor would any industry be allowed to do such a thing for long It is useless to say that conditions in nursing are more acceptable today than they have ever been, young girls do not accept them Without planning, without organisation or leadership, they have used the only weapon to their hand they have become comrades in a stop-out strike

What are the chief factors which deter so many from entering nursing, or; if they enter, from completing the course? We have no figures bearing on this point, and Dr Swindells suggests that we might learn much from a Gallup poll It seems likely, however, that the young girl is daunted by the thought of four years in the restricted atmosphere of the nurses' home, and by the lack of leisure to maintain outside interests and relationships Her parents are discouraged by the poor rewards offered to the qualified nurse—unless, indeed, she forsakes actual nursing for teaching or administration Both are appalled by the burden of domestic work now

4 *Documentary News Letter*, 1945, No 6 p 74
5 Ekhom, K.-A. *Acta med scand* 1945, Suppl 158
6 Allison, F. G *Canad med Ass. J.* 1943, 48, 36.

superimposed on the heavy double task of nursing the sick and working for examinations

We have already suggested[1] that some objections could be met by establishing a practical two year course for all girls entering the profession, and that those who pass an examination at the end of such a course should become state-qualified nurses (SQN) We made it quite clear that this must be a course of *training* not merely a term of hospital service Those who wish to specialise in general nursing or some other branch, or who wish to fit themselves for administrative posts, should then have the opportunity of taking a further more academic course to qualify for the SRN certificate, which might well be raised to the status of a university diploma This proposal has met with some opposition from part of the nursing profession on the grounds that it seeks to degrade the standards of nursing training Nothing could be farther from the truth The first aim is to strip the nursing course of its present irrelevancies and to give the young nurse two years direct intensive training in the care of patients, the second, to raise the standard of the SRN and the standing of the nurse who holds it.

PENICILLIN CREAMS

It is possible in the preparation of penicillin ointments to produce conditions which rapidly destroy the penicillin Losses due to chemical action result from too acid conditions in the base or even more quickly from alkaline conditions These may be inherent properties of the base, or may be produced there during sterilisation through chemical change, but they merit consideration in the choosing or rejecting of a particular base Losses due to bacterial action must also be guarded against While a mixture of oils and water does not make a good medium for bacterial growth, its growth promoting properties are increased by the introduction of penicillin solution, which contains nitrogenous matter Vegetable oils of the ordinary pharmacopœial purity are usually contaminated with a variety of micro-organisms, and ineffective sterilisation may lead to loss of penicillin through the presence of organisms which destroy it Thus the dispensing of penicillin ointments calls for care in the selection of a suitable base, a knowledge of the proper use of sterilisers, and an ability to add a sterile solution of penicillin to the base without contaminating it Hot air and steam sterilisers are not commonly found in country surgeries and pharmacies (the household pressure cooker and gas or electric ovens can be utilised with success), and means to check the hydrogen ion concentration are still less common Without these aids the preparation of satisfactory penicillin ointments is impracticable

In view of these difficulties the arrangements made by the Ministry of Supply with some of the big drug manufacturers for the issue of a ready prepared sterile base of suitable hydrogen ion concentration will be welcomed[2] It is only necessary to add the required amount of solution of the penicillin salt in sterile water to this base to produce an active preparation The preparing of sterilised water and making the necessary dilutions will call for a little ingenuity where pressure or dry sterilisers are not available but much can be done with a clean well boiled graduated syringe and clean new needle to overcome the difficulties of this stage The use of a new needle is important because needles readily harbour extraneous matter Even new needles should be carefully cleaned as anyone who has dealt with the needles in a blood transfusion centre will agree The lumen of needles is best cleaned with a pull through of thick cotton thread.

Of the two types of base in common use for the local application of penicillin, the Ministry of Supply has selected one which has been found satisfactory for many purposes in the last few years In the past ointments were mainly prepared from bases composed of animal or vegetable fats or paraffins chosen largely because of their availability, and their ability to hold the required medicament in contact with the skin or tissues The introduction in the last ten years of newer types of medicaments which act systemically as well as locally called for improved bases, and fortunately these were at hand The "emulsion" bases are solid or semi-solid emulsions in which minute oily globules are dispersed in water or watery globules are dispersed in oil Since water is present in each, a water-soluble medicament can be incorporated in solution and will diffuse out of the base to exert its action The Ministry of Supply type of base consists of a solid oil in water emulsion made by the incorporation of water into melted 'Lanette wax SX' which is a mixture of the sulphuric acid esters of cetyl and stearyl alcohols along with the free alcohols To prepare the base it is only necessary to add water after melting the wax but in practice it is usual to adjust the properties of the base and also economise in the more expensive wax by adding a paraffin or fixed oils Such a base is liable to suffer hydrolysis when autoclaved, with liberation of sulphuric acid, and the hydrogen ion concentration should therefore be checked and if necessary adjusted to pH 6–7 after sterilisation, to avoid rapid decomposition of the added penicillin The other type of base in favour, available under the proprietary name of 'Eucerin LM' is composed of a blend of wool alcohols and paraffin hydrocarbons, and produces an emulsion in which the watery penicillin solution is dispersed in minute droplets through the fats Other bases have been recommended from time to time

There have been complaints regarding the suitability of these bases Lanette wax cream may cause skin irritation the eucerin types are sometimes reluctant to take up water, and sometimes liberate water which will not remix if the cream is frozen as is the custom in one large hospital But on the whole both types of base when properly made possess the necessary properties of blandness freedom from destructive action on the penicillin, ability to be sterilised and remixed easily, and so on

It is curious how little is known about the rate at which penicillin creams liberate their active substance to the tissues or even whether it is liberated at all From the physical nature of oil in water creams one could anticipate too rapid liberation of the medicament, and indeed one fatality has occurred after the application of such a cream containing a large proportion (10%) of sulphanilamide to an extensive burn On the other hand it is difficult to visualise the liberation of medicament at any reasonable rate from the water in-oil types where the watery penicillin globules are locked away in a fatty envelope True, both creams seem to function, but these are important and vital factors which, if fully investigated, should enable us to so modify our bases that we can control the rate of release of the active principles at will

THE VOCATION OF MEDICINE

In his inaugural address at Westminster Hospital medical school on Oct 1 the Archbishop of Canterbury discussed the medical profession from three aspects—the scientific, the social, and the personal On the scientific side while appreciating the organisation of exact knowledge as applied to the human body in itself a most absorbing thing it was comforting, he thought to reflect that man must always be greater than the science he has developed notwithstanding the terror inspired by reflecting upon destruction of the body by physical inventions and of the soul by psychological enterprise Turning to the social aspect Dr Fisher expressed his determination to refrain from all political references and to confine himself to describing the doctor s place in society Only in the doctrine of Christ

1 *Lancet* 1945, i 684
2 The base is supplied by Boots Pure Drug Co Ltd. British Drug Houses Ltd. and Burroughs Wellcome & Co in pots containing about 1 oz

tian society, he said, is a true social life possible The unit of society is the family, and the key position in the medical profession is the family doctor. For this reason the fundamental problem of marriage and sex is one of the most important with which the doctor is called upon to deal Are medical students, he asked, trained to give valuable advice on such matters in their ethical and sociological aspects? On the personal side, true Christian doctrine appreciates that the unit of value is the individual, and in this evaluation doctors join with priests—a vindication that has been the purpose of the war And the war may have inculcated a valuable lesson in respect to a philosophic conception of the meaning of life, a realisation that truth for the most part exists in a fragmentary form, each man specialising in his own particular fragment and knowing little or nothing outside his own field With this, frustration in life proceeds pari passu with agnosticism as the inevitable result The remedy is only to be found in the purpose that governs and controls man—a spiritual value, whether called philosophy or Christian religion

The Archbishop recalled Dean Inge's remark on a similar occasion that he could not see why doctors on qualifying should not, like priests, be ordained Something of a jeu-d'esprit no doubt, but coming from the head of the Church it must have stimulated the neophytes of Westminster Hospital medical school, standing on the threshold of their career, to a realisation that they had indeed embarked upon a vocation—scientific, social, and personal—a vocation that can look on life and death, on good and evil, unafraid

HAPPY ENDING

OLD age is everybody's concern—if only because "we shall all grow old if we live long enough" A booklet[1] issued by the Old People's Welfare Committee, founded in Buckinghamshire early this year, presents ideas and information which other counties and other people interested in geriatrics will value It asks fundamental questions Where should the old spend the last years of life? In the homes of their children? (That is seldom possible in these crowded days) In a home, or a hostel, or an institution? In almshouses? In small houses built especially to meet the needs of old age? The unnamed writer wisely and kindly reviews the alternatives He reminds us why the old poor-house was so much dreaded it meant expulsion from the family circle, the separation of man and wife, and the loss of comforting personal possessions A future pattern is not difficult to foresee "long-term planning envisages a community in which the elderly have their own quarters, and leave the many-roomed houses to their juniors" Some areas have already experimented successfully with flats, houses, and bungalows—separate dwellings where old couples or solitary old people can live among coevals and yet be near their own young people, and the shops and cinemas which provide their daily adventures It is worth noting, in this context, that the London County Council, in developing the Loughton site, in Essex, plans to include among a total of 3850 houses, 108 one-room bungalows suitable for old people. These will be put among other houses, close to shops, churches, schools, restaurants, and a cinema Those who built the old almshouses often set them in the main street, knowing how keen is the interest of the aged in the contemporary scene we share vicariously in the doings of others, and most people who have the leisure like to see the world go round To put old people away behind high walls has never been a kindness Dr Leslie Banks looks forward to cottage estates where the mansion becomes a small hospital, a nurse lives at the lodge, and the old people live in an oval or crescent of self-contained cottages built between the two

Until we can build, however, we must make the best of the present Old people who are lonely can be visited, friends can be found to write to them; they can be given a chance to garden, to live in hostels and take their share in running them, and to join clubs and community centres. In New York an old-age information bureau has been set up for doctors, social workers, and older people themselves The writer commends this idea to London and Sydney

THE POET IN THE DOCTOR

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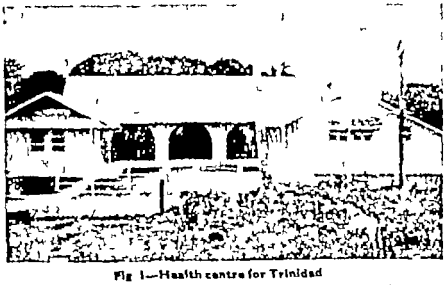

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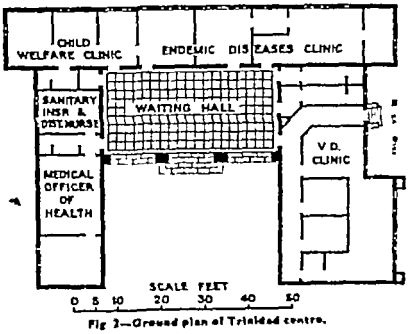

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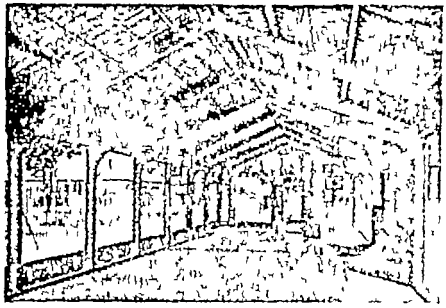

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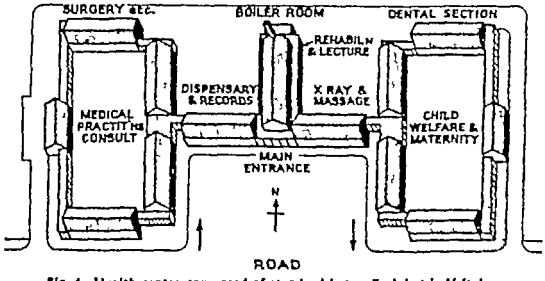

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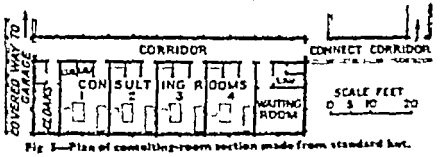

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4 J R Inst Brit Architects, 1942 49 183.

tian society, he said, is a true social life possible The unit of society is the family, and the key position in the medical profession is the family doctor For this reason the fundamental problem of marriage and sex is one of the most important with which the doctor is called upon to deal Are medical students, he asked, trained to give valuable advice on such matters in their ethical and sociological aspects? On the personal side, true Christian doctrine appreciates that the unit of value is the individual, and in this evaluation doctors join with priests—a vindication that has been the purpose of the war. And the war may have inculcated a valuable lesson in respect to a philosophic conception of the meaning of life, a realisation that truth for the most part exists in a fragmentary form, each man specialising in his own particular fragment and knowing little or nothing outside his own field. With this, frustration in life proceeds pari passu with agnosticism as the inevitable result The remedy is only to be found in the purpose that governs and controls man—a spiritual value, whether called philosophy or Christian religion

The Archbishop recalled Dean Inge's remark on a similar occasion that he could not see why doctors on qualifying should not, like priests, be ordained. Something of a jeu-d'esprit no doubt, but coming from the head of the Church it must have stimulated the neophytes of Westminster Hospital medical school, standing on the threshold of their career, to a realisation that they had indeed embarked upon a vocation—scientific, social, and personal—a vocation that can look on life and death, on good and evil, unafraid

HAPPY ENDING

OLD age is everybody's concern—if only because "we shall all grow old if we live long enough" A booklet[1] issued by the Old People's Welfare Committee, founded in Buckinghamshire early this year, presents ideas and information which other counties and other people interested in geriatrics will value It asks fundamental questions Where should the old spend the last years of life? In the homes of their children? (That is seldom possible in these crowded days) In a home, or a hostel, or an institution? In almshouses? In small houses built especially to meet the needs of old age? The unnamed writer wisely and kindly reviews the alternatives He reminds us why the old poor-house was so much dreaded it meant expulsion from the family circle, the separation of man and wife, and the loss of comforting personal possessions A future pattern is not difficult to foresee "long-term planning envisages a community in which the elderly have their own quarters, and leave the many-roomed houses to their juniors" Some areas have already experimented successfully with flats, houses, and bungalows—separate dwellings where old couples or solitary old people can live among coevals and yet be near their own young people, and the shops and cinemas which provide their daily adventures It is worth noting, in this context, that the London County Council, in developing the Loughton site, in Essex, plans to include among a total of 3850 houses, 108 one-room bungalows suitable for old people These will be put among other houses, close to shops, churches, schools, restaurants, and a cinema Those who built the old almshouses often set them in the main street knowing how keen is the interest of the aged in the contemporary scene we share vicariously in the doings of others, and most people who have the leisure like to see the world go round To put old people away behind high walls has never been a kindness Dr Leslie Banks looks forward to cottage estates where the mansion becomes a small hospital, a nurse lives at the lodge, and the old people live in an oval or crescent of self-contained cottages built between the two

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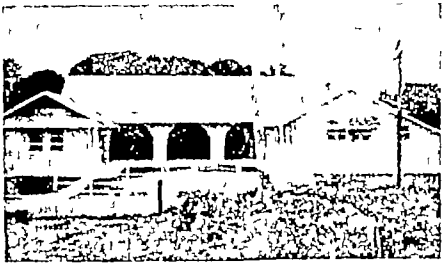

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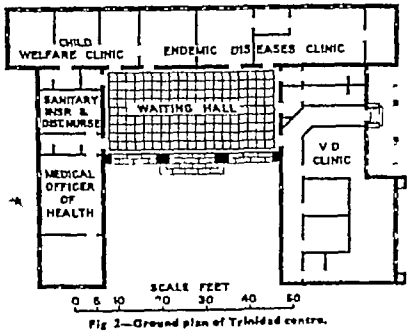

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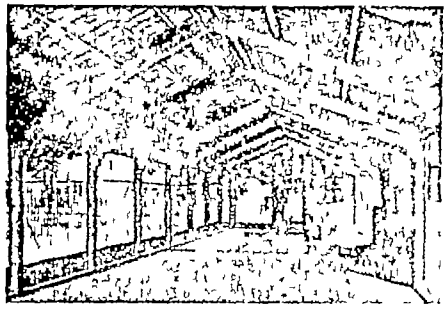

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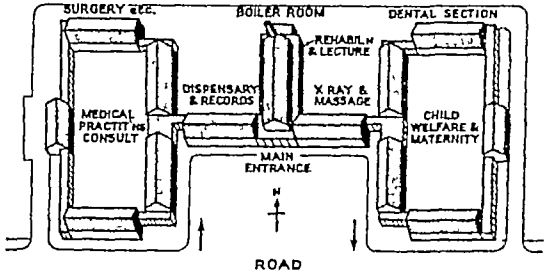

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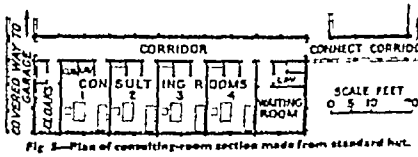

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4 J I Ind Bld (Lond), 1945 49 195

Special Articles

OCCUPATIONAL ADJUSTMENT OF THE BLIND

ERIC FARMER, M A CAMB

READER IN INDUSTRIAL PSYCHOLOGY IN THE UNIVERSITY OF CAMBRIDGE

PSYCHOLOGICAL methods of vocational guidance can obviously play an important part in the occupational adjustment of the blind, or in fact of any disabled person Yet the volume of work on this subject is not very great In the last thirty years psychologists have been busy validating methods of mental measurement, and it is only natural that they should have worked on normal populations The success that has attended this branch of scientific study now makes it possible to carry out work more extensively among abnormal populations, such as the war-disabled, whose needs are at present urgent In this paper I propose to deal with the blind only, but it is to be hoped that other kinds of disablement will be systematically studied by psychologists, for there is probably no field where their services will be of more value

CLASSIFICATION OF THE BLIND

For purposes of clear thought in assessing the value of mental measurements among the blind, it is convenient to divide them into certain categories.

The first category is those *blind in infancy* Such persons are often spoken of as being born blind This rarely happens, though many lose their sight so early in infancy as to have had no visual images that they can retain. Their whole mental life must therefore be built on non-visual perception, without the aid of remembered visual imagery Most of these persons will enter a school for the blind at an early age, where they will receive systematic education and training specially suitable for them. Training for any skill is a lengthy process among the blind, and it also plays a greater part in proficient performance among them than among the sighted Hence children trained from infancy in a blind-school may easily reach a higher standard of educational or manipulative performance during their period at school than those trained in the same school who lost their sight at an age when they had already had a full experience of visual imagery

Much blindness in infancy can be averted by medical precautions, and these measures are more likely to be carried out by intelligent parents than others Since intelligence is to some extent hereditary, the average mental level of those blind in infancy is lower than the normal for the whole population It has already been noticed in America that the intelligence level of those blind in infancy is tending to fall, and this is taken to mean that this population is drawn more and more from the less intelligent parents as medical preventive measures come to be used more and more by intelligent parents

Those who become *blind through illness* at any period after they have had effective experience of visual imagery form another category of the blind. The age of entering into blindness for this category is important. If they enter while young children or adolescents, they may have the necessary capacity to benefit from an education specially fitted for the blind If they enter it in middle age they may find learning new skills too difficult The loss of sight in some in this category may be associated with general ill health, and in so far as this is so they will not tend to be so robust as the general population. Many in this category lose their sight gradually, and there is some evidence to show that this may affect their adjustment to blindness and their capacity to learn the skills involved in this adjustment. They cling to the last remnants of sight and hope against hope that they may get better, and thus refuse to accept blindness and adapt themselves to new modes of behaviour.

Finally, there are those who are *traumatically blinded* Most of these are war casualties. Among the civil population those blinded by war are distributed almost normally among the population and among them are found people of all ages and of either sex Blind Service-men are not a normal sample of the population The lowest levels of intelligence are not found among them, because such men would not have been admitted to the Forces The highest levels of intelligence are fewer than in the total population, since reservation has excluded from combatant service some of those following the highest types of occupation. The age-range of these men is also skewed, there being a preponderance of healthy young men at their most physically, mentally, and emotionally active period

The *partially blind* are found in all of these categories Such people have sufficient defect of vision to justify them being officially classified as blind Some can detect objects on the periphery but not in the central field of vision; others may have partial central vision which varies in capacity from detecting large objects to being able to distinguish light from dark Partial vision can play an important part in orientation, but people with similar degrees of partial vision vary considerably in their capacity to use it. This suggests that selection is involved to a large extent in the vision of the partially blind, and that the ability to use their sight may depend more on meaningful attention than on visual capacity Enough has been said to show how heterogeneous is the population of the blind and how much caution we should use before accepting experimental results based on limited and often ill-defined groups The blind have only their blindness in common, in all other factors they may differ, and it is these other factors which are so important in their occupational adjustment.

INTELLIGENCE TESTS—ORIENTATION

A fair amount of work has been done on measuring the intelligence of blind children The results of some of the experiments are rather inconclusive, for the experimental populations have not been clearly defined, and we know neither how many had partial vision nor the age of entering into blindness. Both these factors must affect performance as a measure of pure intelligence, they need not, however, affect test performance if it is regarded only as a measure of the capacity to perform certain tasks. To use intelligence tests to compare directly the mental ability of the blind with that of the sighted appears a doubtful procedure, for no test can be a fair measure of ability for those depending solely on non-visual percepts and for those with normal vision.

The method Miss I W. Langon is pursuing is a more reliable technique. She is trying to construct a test which will give normal age-distribution among blind children similar to that given by the Binet test among sighted children In so far as she is successful over the whole age-range—and her present results give every indication that she will be—she will be able to say for a blind child where his score falls on the frequency distribution curve. Since there is a significant correlation between intelligence tests, it follows that those whose scores fall at any point on the normal curve of one test have an intelligence which does not differ significantly from that of those whose score falls at a similar point on the curve of another test which gives a normal age-distribution In this way a fair measure of mental ability among the blind comparable with that of the sighted will be available

Several experiments have been carried out on the orientation of the blind, mainly to determine the factors involved in it The results are contradictory, which seems almost inevitable from the experimental technique adopted This has usually consisted of experimentally eliminating a single receptor mechanism, such as smell or hearing, as a result of which orientation deteriorates This is taken to mean that orientation is mainly based on the eliminated receptor. These results are equally open to the interpretation that orientation is a complex factor depending on the interaction of several receptor mechanisms; and that, when one of these is temporarily out of action, the balance of the blind man's perceptual field is disturbed Possibly if he had time to adjust to the altered circumstances he might be able to reach a satisfactory degree of orientation based on fewer perceptual cues, but this is not possible under normal experimental conditions

The actual basis of orientation is not so important vocationally as variations in the capacity, and these are considerable It is probable that these variations are not primarily determined by differences in sensory acuity but by differences in the capacity to select and interpret meaningful cues from a total presentation and

fit them into the mental continuum The fact that blind persons often do not distinguish as disparate the points of a compass far wider apart than the dots of the Braille alphabet, while being able to read Braille with ease, shows how much meaning must enter into these perceptual cues

S P Hayes[1] has done a series of carefully controlled experiments on what he calls the 'vicariate of the senses"—i e , the commonly held belief that the non-visual sensory perceptors are more sensitive among the blind than among the sighted The general conclusion drawn from these experiments and others in the same field is that the non visual sensory receptors of the blind are not more sensitive than those of the sighted : in fact, in some cases they are less so Touch, when measured at a sensory level, is often inferior among the blind because the skin at the finger-tips is thickened by constant use. The blind do, however, after training and experience, develop an amazing capacity for exploring and adjusting to the outside world , but this is not because of their greater sensory acuity but because they have to pay attention to non visual perceptual cues which can be largely disregarded by the sighted owing to their predominant reliance on visual cues

Some of the experiments I have done and discussions I have had with cultured blind persons indicate that conscious inference enters more in the non visual perceptual field of the blind than the more immediate type of recognition involved in visual perception If this is so, it means that intelligence is more concerned with orientation among the blind than among the sighted There is considerable variation in capacity for orientation among the blind, and these variations play a dominant part in their occupational adjustment It is important, therefore, to discover the mental factors involved in orientation. All the work so far goes to show that these are more likely to be found at the level of meaningful selection and inference than at that of *sensory acuity*

SUGGESTED TESTS

A brief description of some of the tests I have devised will show the line of approach I think may be useful These tests are meant only for adults who have been traumatically blinded , they would probably not be suitable for other categories of blind persons, for remembered visual imagery is involved in some of the tests.

(1) A simple oral intelligence test suitable for differentiating roughly between those with the mental ability suitable for unskilled, semi skilled, and skilled occupations. This test is based largely on the experience I have gained in testing the intelligence of adults for occupational ability It involves repetition of numbers, analogies, opposites, simple mental arithmetic, remembering the details of letters These latter two questions involve special ability and knowledge, but they embrace factors vital to the blind man's adjustment to the sighted world and are therefore important vocationally

(2) A more difficult mental test, suitable only for those who have done well on the first test and may be capable of undertaking important administrative posts This consists of directions to be precisely carried out, instructions to be carried out with varying choice of means, difficult reasoning, and adjustment to social situations

(3) The following tests are all designed as a preliminary attempt to examine variations in orientation :

(a) A cube-construction test depending on tactual cues
(b) A form board depending on tactual cues
(c) An apparatus for measuring judgment of distance depending on touch and kinæsthetic sensation
(d) An apparatus for judging size depending on touch
(e) An apparatus for judging weight
(f) An apparatus to measure accuracy of movement depending solely on kinæsthetic sensation

These tests have been tried in the laboratory and on a few blind persons They appear to differentiate significantly between individuals and to correspond in the blind to what is known of their general performance The data are not yet sufficient to warrant definite conclusions but they are sufficient to warrant using the tests experimentally

It will be difficult to get satisfactory criteria of the value of the tests because of the heterogeneity of the blind population and the various types of occupations they enter The best that can be expected will be something like the criteria for vocational guidance as opposed to those of vocational selection It is an important matter to decide a blinded man's occupation because of the lengthy training that is necessary If, as the training proceeds, it is found that he is unsuitable for the occupation, another lengthy period of training must be started. This is a disappointing experience for the men, for they naturally want to become self supporting as soon as possible and return to their normal family life It is probable that the use of psychological tests will help in deciding what occupation a man should train for and will lessen the chance of failure Failure to complete a training course not only wastes much time but also in the blind may easily lead to a feeling of frustration which it is important to avoid This failure may be attributed to their blindness and lead to a depressed attitude towards learning another occupation Failure to learn the skill necessary for an occupation may, in fact, be more determined by mental qualities than by blindness , if these were systematically examined before starting the training for an occupation, much disappointment to the blind might be saved

EMOTIONAL ADJUSTMENT AND EMPLOYMENT

An essential part of the occupational adjustment of the blind is at the emotional level Sudden blindness is a great shock to a young and healthy man with his natural feelings of independence. For the most part the adjustment of St Dunstan's men is amazing This is largely due to the sensible way in which the men are treated and the atmosphere of cheerful independence that permeates the place

An emotional shock, such as blindness may produce, accentuates the characteristics of the individual and brings to the surface latent aspects of personality It may also precipitate certain conflicts which may not have disturbed the previous life of the blinded but may become very crippling under the added strain of blindness Such men need the help of a psychiatrist if they are to make a satisfactory adjustment

For the most part the blinded show a degree of well-balanced courage which is a magnificent example of human nature at its best This courageous attitude, if affected by emotional disorganisation, may develop into over-compensation and take a fantasy form, instead of the more useful form of well-directed effort on training and the overcoming of difficulties.

The more recessive type of character learns naturally to adjust to blindness by quiet application to work and a well balanced limitation of his demands on life With the emotionally disturbed this attitude may easily develop into a retreatist attitude which will add greatly to the difficulty of occupational and social adjustment

Perhaps the most surprising thing about St Dunstan's is the relatively small number of men who are emotionally disturbed when one might have expected it to be otherwise Coming to St Dunstan's as soon as they are medically in the condition to do so is an important factor in their emotional rehabilitation If an unduly long period elapses between entering into blindness and coming under expert care, men may easily fall into a false emotional attitude towards their blindness which may retard their adjustment

Adjustment of the blind to many simple routine occupations is not difficult Many blind persons are working in ordinary factories and their output is not less than that of the sighted and is often greater, probably because they are not so easily distracted Many blind persons of superior mental and social ability have held and are holding important administrative posts Such men should have the kind of ability that would raise them to positions carrying a private secretary They also need considerable capacity in orientation so as to fit naturally into the changing circumstances of their environment There is greater difficulty in placing men whose qualifications suit them for occupations in the middle range, but this is being systematically undertaken by St Dunstan's One of the difficulties is the prejudice of employers There are however, many notable exceptions and every blind man successfully placed increases the chances of placing others. This is overcome by seeing the extent to which adjust if properly selected trained and opportunities of employment

1 Contributions to a Psychology of Blindness New York American Foundation for the Blind 1941

In England Now

A Running Commentary by Peripatetic Correspondents

NAPLES has already provided the one dramatic epidemic of the war, and my bet is that it will be responsible for the next Two years after liberation Naples is still in a shocking state, materially, morally, and hygienically. Dust, dirt, smells, flies, lice, mosquitoes, and sandflies are everywhere The water-supply is intermittent, and what negative pressure and back-syphonage does in the interval appears to be nobody's business Italy abounds at least in labour and stone, but there are still pot-holes in the roads and pavements, and little attempt at repair or rebuilding seems to have been made The hundreds of small children (who never seem to go to bed) beg, try to pick your pocket, openly offer black-market cigarettes, and steal anything left unwatched for a moment A naval officer's wife, riding in a jeep with her husband, had her handbag snatched off her lap as the jeep slowed up round a corner, An UNRRA nurse, convoying some penicillin in a jeep, refused to let a gang of youths board it and was being roughly handled when saved by the appearance of a truck with American soldiers. Families with children are still living in caves used as air-raid shelters A hospital for abandoned children has a death-rate of 70%, and 40% of the infants admitted are syphilitic "See Naples and die" may be all too likely.

* * *

On the whole, Poona has taken the Peace very well. There have, of course, been a few overt complaints in cases of special hardship—from Indian contractors, who see their market slipping, or from VIPs, whose red tabs have suddenly acquired an uncomfortable instability. But the general mood has been one of quiet endeavour—making the best of a bad job, and saving what we can from the wreck. On VJ night, I happened to be visiting a friend in a club which is not one of my usual haunts, and it was touching to see how pluckily the old fellows were taking it At the end of the last war, if one can believe Philip Gosse's *A Naturalist goes to War*, there were some signs of weakness; a permanent member said "Good evening" to a temporary member But such shameful scenes have not been repeated, and anyone who turns up to dinner in a lounge suit is quite properly put in the "dirty room," away from the others

* * *

"*Cedant arma togæ*," said Cicero, "*concedat laurea laudi*" and did not, apparently, see any difficulty in the change Cincinnatus too, having won his battle, went back to his plough and, no doubt, to some rough smock which fitted him well enough Wellington's generals in the Peninsula would have little difficulty in the transition from military to civil clothing, on their campaigns they wore frock-coats of their own devising, and could retain them in the days of peace But now there seems to be some difficulty for the returning warrior Twice in one week there have been anguished letters in the press An army marches on its stomach and these letters show that the British is a great army A correspondent of the *Times* protested against being directed, on demobilisation, to the clothing department marked "42, and portly"; a writer to the *British Medical Journal* complained that he could not get into his civilian clothes when he left the Forces, like the man in Dickens, he was not able to see his lower regions, when standing, after some years of military service Our soldiers seem to be modelled on the generous Falstaff rather than the lean Cassius, or the scrawny Quixote To Cicero this would have meant little, a toga is designed to fit any figure · a twitch here or there, a sweep of the arm to throw the fold over an ample shoulder, and the thing is done Waistline measurements caused no pangs Indeed a majestic portliness goes well with a toga, as Charles James Fox found out, after his service in the Home Guard of the time—judging by his statue in Bloomsbury Square. But nowadays nobody solves his problem like that The doctor who wrote to the *British Medical Journal* was constrained to a 28-day fast, taking nothing but fluids, an alkali mixture, and some vitamin preparations He lost 30 lb, felt reasonably fit, and regained that prospect of his nether limbs which he had lost awhile. Peace had its victory, no less renowned than war, and what a welcome home he must have received from those who collected his rations and his points, *concedat laurea laudi*.

* * *

Over the courthouse floats a great Union Jack, and an imposing cordon of military police controls the crowd of inquisitive Lüneburgers The courtroom is impressive with its floodlights, microphones, interpreters, and cosmopolitan press gallery. The Bench, consisting of five senior officers in sparkling Service dress with caps, and the Deputy Judge Advocate General in wig and gown, perfectly sustains the dignity of British institutions The long array of defending officers symbolises the scrupulous—almost too scrupulous—fairness of British law

Opinions differ about the appearance of the Belsen criminals I thought they were the foulest, most nauseating collection of humanity that I had ever seen. Photographs give no inkling of how revolting they appear in the flesh The only two who in my humble opinion show the slightest sign of finer features are oddly enough the chief offenders, Kramer and Klein. They obviously have more intelligence and education than the rest

In the last twelve years the sadists and the mentally-backward have terrorised their fellow-countrymen, and they will do so again the moment the Allies leave the country The problem of Germany is not political or economic it is psychiatric

* * *

Back in 1943 my friend the Major from the War Office showed me a newspaper account of police-court proceedings It read something like this: "When arrested, the accused declared that he was a Major from the War Office" It pleased the real major to see this incident reported in a fashion which plainly conveyed that the unhappy accused suffered delusions of grandeur. His approval of lay reactions to War Office Majors was increased by an incident in the film, *I Live in Grosvenor Square*. Solid, upright policemen guarding the room where election votes were being counted gave way to allow the entry of an insistent gentleman as soon as he disclosed that he was "a Major from the War Office" My friend was not surprised at this—he had never tired of saying that he and his like held all the power and completed all the actions while Colonels, Brigadiers, and Generals were put up to impress the public, mainly by wearing red tabs and occupying the first-class sleepers But frankly his self-approval began to irritate me when he gloated over the appearance of a War Office Major in the *Daily Mirror* beside Jane herself. Here at last was real fame, he thought—a fitting recognition of a gallant type But he had it coming to him, for at last perspectives have altered Jane's major is proved an impostor and at the time of writing the ridiculous Captain Cod seems cast for complete triumph I waited for a good chance to rub this into the Major from the War Office, whose arrogance had increased beyond endurance But he must have read the signs correctly for he hurriedly got himself demobilised and I learn that he now hopes to attend postgraduate classes with a view to qualifying as a psychiatrist

* * *

Recently I met a man who had just been released from a prison-camp in Thailand, where he had been since the fall of Singapore He and his companions got off lightly as far as actual atrocities were concerned As an MO, he had been in fairly large camps most of the time, and the worst incidents seem to have been in small detachments under the care of irresponsible junior officers or NCOs But the feeding had been very bad, and official contact with the outside world was absent, though, with that amazing ingenuity which one remembers reading of in escape stories of the last war, they had rigged up a wireless from carefully concealed parts It was by this means that they heard of penicillin—the "wonder-drug"—but of its applications they had no inkling when first released, for they had thought it was some kind of secret weapon for use against the Japs.

* * *

Come on, you Classicists! What does this notice in a main street of Athens mean? "ΟΔΟΣ ΟΥΙΝΣΤΩΝ ΤΕΡΤΣΙΑ"

Letters to the Editor

GAS-GANGRENE

SIR,—The articles by Majors MacLennan and Macfarlane (Sept. 8 and 15) are of particular interest to me in view of the similarity of their findings with *Cl welchii* toxin and antitoxin to mine with *C diphtheriæ* toxin and antitoxin (*J Path Bact.* 1940, 51, 317, *Lancet* 1941, i, 205; *Ulster med. J* 1943, 12, 5) I have shown that in the full development of the toxæmia of diphtheria as found in the hypertoxic case two components of toxin are operative The first of these, substance A, is the guineapig lethal factor of laboratory toxin, the second, substance B, is a factor which promotes the distribution of the lethal factor through and into the tissues, enhancing its action and intensifying the toxæmia without however, altering the minimum lethal dose as determined by immunologists in the laboratory

For some time I have regarded clinical hypertoxic diphtheria as a disease closely akin to gas-gangrene in its pathological features. In both there is a local lesion, accompanied by necrosis and massive œdema, and profound general toxæmia which is little amenable to treatment with commercial antitoxin. In both the heart is seriously involved The details of the toxæmic picture are naturally different in some other respects, since the pathological activities of the lethal factors of the two toxins are demonstrably different in the laboratory The absence of gas in hypertoxic diphtheria is simply due to the fact that *C diphtheriæ* does not produce gas during growth, whereas *Cl welchii* does

When I originally started to investigate the toxæmia of diphtheria I examined serum taken from a number of cases in a profound state of toxæmia, both before and after the administration of antitoxin but in no case was it possible to demonstrate any toxin, although the test used—intradermal inoculation in the guineapig—is probably 50–100 times more delicate than that used by MacLennan and Macfarlane to detect *Cl welchii* alpha toxin By comparison, therefore, it is not surprising that laboratory tests failed to reveal gas-gangrene toxin in the serum of their cases. I also extracted the tissues of the throat in a case of hypertoxic diphtheria after death and recovered from them rather less than one guineapig minimum lethal dose

But these findings scarcely warrant the assumption that the classical toxins play no part in the disease So far as diphtheria is concerned the amount of the guineapig-lethal factor necessary to induce toxæmia is very small provided that an adjuvant—be it collagenase or hyaluronidase or some similar factor causing tissue penetration—is also present It is the amount of this second substance which determines, in conjunction with quite minute amounts of the first, the severity of the toxæmia and its response to antitoxin It is interesting, in this connexion, to note that Dr McNally and I have found in our experiments (*Lancet* 1941, i 555; *Irish J med Sci* 1941, p 230) that *Cl welchii* toxin, in amounts of no toxic significance acts as an excellent adjuvant to sublethal doses of diphtheria toxin and reproduces the hypertoxic type of diphtheria in guineapigs. The non toxic but tissue-penetrating component of *Cl welchii* acts in the same way as substance B produced by the diphtheria bacillus

Macfarlane and MacLennan suggest that it may be the breakdown products of muscle liberated by infection of that tissue which are responsible for the toxæmia of gas-gangrene, and cite in support of this contention the slight toxæmia associated with *Cl welchii* cellulitis and brain infection Another interpretation is, however, possible in the light of simple experimental observation It is well known that *Cl welchii* produces little demonstrable alpha toxin when grown in ordinary nutrient broth but produces this toxin in greater or less amounts according to the strain used when grown in the presence of minced meat This fact is recognised in the routine of commercial laboratories where *Cl welchii* toxin is manufactured by growing the organism in meat broth I have tested it quite simply by growing the organism in the thioglycollic acid broth described by me (*J Path Bact* 1937 45, 541) and in Robertson's meat broth in parallel With casual strains isolated from milk I have observed no toxin formation in the thioglycollic acid-broth medium and well marked toxin formation in Robertson's meat medium It is, therefore, probable that the toxæmia which accompanies infection of muscle is due to the production of alpha toxin when the organism grows in muscle But the amount necessary to cause toxæmia of a most intense character may be very small as my experience with the guineapig lethal factor of diphtheria toxin shows, provided that an adjuvant to its action, such as is found in *Cl welchii* toxins, be present as well It is worth mentioning that *C diphtheriæ* infection of certain tissues such as the skin is associated with little toxæmia, since one would more readily suggest that the organism in this form of infection elaborates little toxin in the skin than seek to attribute the toxæmia of the commoner form of the disease to the products of disintegration of the fauces!

In my studies of toxins and antitoxins I have been struck by the lack of avidity of gas gangrene antitoxins They are probably among the least avid of all antitoxins as might be expected from the constitution of the toxins they are required to neutralise I have shown with diphtheria antitoxin that an excess of the second constituent (substance B) in the toxin renders the antitoxin non-avid; so it is not surprising, in view of the observations of MacLennan and Macfarlane that gas gangrene antitoxins lack avidity Dr McNally and I (loc cit) have obtained evidence that *Cl welchii* toxin causes dissociation of diphtheria toxin from combination with its antitoxin I suggest that what is required for the successful treatment of *Cl welchii* infections is an avid antitoxin similar to that required for the treatment of hypertoxic diphtheria Modern antitoxins standardised in laboratory units which have little relation to clinical requirements, are, in most cases, of low avidity and of correspondingly low therapeutic potency

Trinity College, Dublin R A Q O'MEARA.

SIR,—I have read with interest Dr Robb-Smith's article on tissue changes induced by *Cl welchii* type A filtrates, in your issue of Sept 22 As a surgeon I am not qualified to comment on the valuable experimental work which he has carried out but, as a clinician there are several comments I would like to make arising from his paper

I like the term myonecrosis in lieu of myositis, it very aptly describes the condition found at operation—i e, a mass of necrotic muscle It bears out my contention that gas gangrene is an infection of dead muscle and not as MacLennan holds, that it is essentially an infection of living muscle

I have pointed out (*Brit med J* May 12, 1945, p 650) that arterial damage by cutting off the blood supply to muscle, was essential for the establishment of gas gangrene, and have published 16 cases in support of this theory The mass of dead muscle forms a sequestrum in which any organism can develop without difficulty Since the sequestrum is cut off from all blood-supply, parenteral administration of drugs is of no avail. The failure of penicillin to stem the disease is a glaring example when we consider it is specific to the clostridium

Robb-Smith freely admits the absence of inflammatory reaction to gas-gangrene To quote his paper at random, "it will be necessary to discuss a remarkable feature of the local changes in gas gangrenous muscle—the virtual absence of inflammatory reaction"; and again, there is an almost complete absence of a fibrin network in clostridial myonecrosis and no vascular hyperæmia" It is not surprising that these facts have emerged How can an inflammatory reaction take place in dead muscle when there are no blood vessels to carry the leucocytes and fibrin to the part? It is also not surprising to find disintegrated leucocytes in the midst of the sequestrum for their nutriment and retreat have been cut off and they are left to die The position is analogous to the calcium in a bone sequestrum which is left stranded If the infection had started in living muscle inflammatory reaction would surely be present Nevertheless Robb-Smith flirts with the hypothesis that infection of living muscle is a possibility To quote him again "It has been shown that it is possible to reproduce in vitro with bacteria free extracts, the histological changes in the muscle in human gas gangrene with the exception of œdema and gas formation" and but the proximate conditions that allow spores introduced

into wounds to proliferate and form toxins are not clearly understood"

Such an hypothesis would not be substantiated by any war surgeon. Clostridia are ubiquitous and no wound in peace or war would be safe from this infection, the disease would be rampant The war surgeon has come to realise the truth in the slogan "No dead muscle—no gas-gangrene" This was borne out in the war of 1914–18. In the early stages, when wounds were not opened up and excised, gas-gangrene was most prevalent, but as soon as this was rectified gas-gangrene almost disappeared

Finally, Robb-Smith recommends the injection of antiserum locally around the wound when it has been impossible to remove all necrotic muscle If the sequestrum is present, clostridia will wallow in it, and I can see no beneficial effects from antiserum injected into its midst If the sequestrum has been removed, there is no necessity for antiserum, for the remaining clostridia are soon overpowered by the body defences If Macfarlane and MacLennan's contention be true—that the systemic symptoms of gas-gangrene are not due to circulating toxins—then antiserum is of no avail.

If a muscle sequestrum be present, it must *all* be removed at operation regardless of disability to follow. If the surgeon does not do this, nature will in her own good time, if the patient is fortunate enough to survive. Dead muscle can never be brought to life again and failure to remove it at operation is only inviting disaster

Hereford R WOOD POWER

SIR,—In your issues of Sept 8 and 15 Majors Macfarlane and MacLennan suggest that the general toxæmia of gas-gangrene produced by *Cl welchii* is not due to α-toxin but to products derived from disintegrating tissue They identify in *Cl welchii* toxic filtrate, an enzyme "collagenase," which they state is directly involved in the muscle destruction in gas-gangrene They further suggest that an antitoxin or toxoid designed to confer a high anticollagenase immunity might be more effective than the present methods which are judged by their α-antitoxin effect. *Cl welchii* A produces a number of antigens. α-toxin, θ-hæmolysin, hyaluronidase, collagenase, and no doubt others not yet identified. The relative importance of the first three of these antigens in experimental gas-gangrene, and of their respective antibodies in the control of the disease, has been the subject of a series of investigations during recent years,[1] and the results have shown that α-toxin plays the most important part in infection and that α-antitoxin is the significant antibody in the control of the disease

In view of the work of Macfarlane and MacLennan, a similar study has now been made of the protective properties of anticollagenase in experimental gas-gangrene Two *Cl welchii* antisera, kindly supplied and assayed by Dr C L Oakley of the Wellcome Physiological Research Laboratories, were tested for their protective action against gas-gangrene produced in guineapigs by each of four different strains of *Cl welchii* A. One of the antisera contained anticollagenase but no α-antitoxin, while the other contained α-antitoxin but no anticollagenase. The serum was administered to the animals 16 hours before infection Results of the experiments showed that:

(1) Serum containing anticollagenase and no α-antitoxin was unable to protect guineapigs against gas gangrene produced by the smallest dose of *Cl welchii* A, which caused death in untreated animals

(2) Serum containing α-antitoxin and no anticollagenase was effective in protecting guineapigs against gas gangrene produced by at least 1000 lethal doses of *Cl welchii* A.

(3) A mixture of anticollagenase and α-antitoxin gave no better protection against the disease than α-antitoxin alone

It therefore appears that in the control of experimental gas-gangrene, produced in guineapigs by *Cl welchii* A, α-antitoxin is of prime importance It is also reasonable to suppose that α-toxin plays the most important part in the infectious process, and while it is recognised that the rapid spread of the disease may be associated with hyaluronidase production, and that muscle destruction may be a result of the action of collagenase, there is so far no evidence to support the view that either of these enzymes plays any substantial part in the genesis of fatal gas-gangrene

London NW3 D G EVANS

Evans D G. *Brit J. exp Path* 1943, 24 81, 1946, 26 104, *J Path. Bact* 1943, 55, 427, 1945, 57, 75

THE NURSING CRISIS

SIR,—The letter from Sister Bateman (Sept. 22) demands attention as coming from one who by her own experience knows where the shoe pinches That hospitals are increasingly and admittedly failing to attract entrants to both the nursing and domestic sides shows that there is something fundamentally wrong. An easy reaction is to blame it on "the modern girl"—which certainly saves one the trouble of thinking, but is rather like grandfather over again. "In my time . ." The elders of each generation have talked like that

Surely it is time to examine the situation from a new angle and try to find out the causes Sister Bateman relates some, others suggest themselves at once to anyone familiar with the way in which hospitals are run. What other industry today attempts to cover a twenty-four-hour day on two shifts? Why must nursing students be required to live in, and be under some sort of control for twenty-four hours in the day? Other students are not And why, as students, must they do so many purely domestic duties, which could be much better done by someone trained or training for such work? These, as we all know, keep them from their first duty of attending to the patients

My purpose, however, is not to theorise as to why hospitals cannot attract entrants but to suggest that the Institute of Public Opinion be asked to make an inquiry and find out from the girls themselves why they won't take up nursing or hospital domestic work A Gallup poll would, I think, throw light on the question and save us from continued fumbling To get the history before attempting diagnosis or treatment is a sound way. The young are not always wrong in what they want, and they are showing that they do not want nursing under present conditions

Grimsby S W SWINDELLS

SHOULD A BRACHIAL PLEXUS INJURY BE EXPLORED?

SIR,—The question asked by Mr Hambly in giving a title to his paper of Sept. 22 is an important one, to which many of us would like to know the answer As Mr Hambly says, the general opinion is that exploration of wounds of the brachial plexus is not worth while; but he evidently thinks as I do that a proper judgment ought to be based on something more substantial than odd impressions I cannot remember the details of our conversation last October, but I think I suggested to him that the proper approach was to explore all serious open injuries of the brachial plexus to determine how many presented lesions (*a*) capable of surgical repair, (*b*) incapable of repair, or (*c*) not requiring repair The operative findings and procedures would, of course, be fully documented, and the cases observed subsequently at regular intervals so that in due course we should know whether those in which repair had been carried out showed sufficient recovery to justify what had been done, and whether those in which the damaged parts of the plexus were in continuity, and not sufficiently scarred to warrant resection and suture, had shown the anticipated degree of recovery. Clearly this is a tedious inquiry but one that must be made before we can know what, if anything, we can offer our patients, and I hoped that a substantial contribution would be made by Mr. Hambly

It is therefore disappointing, when one reads his case-reports, to find no mention of the dates of injury, operation, or recovery, and so little neurological information as to be worthless One cannot, however, help suspecting that in case 8 operation can hardly have been necessary since the rapidity of recovery suggests that a non-degenerative lesion (neurapraxia) was present, and would have recovered spontaneously anyway.

The title of the paper suggests that Mr Hambly was out to give us some big news As it is, the only arresting piece of information is that in cases of irreparable brachial plexus paralysis arthrodesis of many joints is preferable to amputation followed by the fitting of an artificial limb. He seems to be fairly certain about this; but how does he know—may we have the evidence? No doubt he will recall the discussion at Oxford last year when Mr Hendry described his cases (I think there were two) in which he had arthrodesed a number of joints in a paralysed limb and thought the results better than could be obtained by amputation and prosthesis But I doubt whether Mr

Hendry was expressing more than a personal preference Has anyone yet made a careful comparison of the cases treated by these two very different methods? If Mr Hambly has done so we shall be greatly in his debt for providing the answer to a question that bothers me every time I meet one of these unfortunate patients with hopeless brachial plexus paralysis But if he is giving us only an opinion, then his is no better than mine, and mine, until it is based on evidence, is almost worthless

Wingfield Morris Orthopaedic Hospital Oxford

H. J SEDDON

THE LABOUR PARTY AND A NATIONAL HEALTH SERVICE

SIR,—The victory of the Labour Party at the general election has brought a new factor into the negotiations for a National Health Service For the first time a Government is in power which is pledged to provide a complete medical service for all sections of the community, *and it is to be presumed that it will at least put* the main lines of its policy into effect Yet, judging by what is said, many doctors are far from adequately informed of what the Labour Party policy is For instance, some believe that it is intended to abolish a patient's freedom to choose his own doctor, whereas the policy states: "patients should be able to change their doctors if dissatisfied, and have a choice of an alternative."

Consequently we would like to draw attention to the fact that the Labour policy for health has been published in a pamphlet *National Service for Health*, which can be obtained from the Socialist Medical Association We recognise that at this stage no policy can be final and that much constructive work will be required before a perfect service can be obtained We hope that all doctors who have the same aim as we have—namely the provision of the best attention that science makes possible for all, irrespective of economic position, and the best conditions and full professional freedom for doctors and other health workers—will be able to coöperate in achieving it

SOMERVILLE HASTINGS
President

Socialist Medical Association
35 Long Acre London, W.C1

HORACE JOULES,
D STARK MURRAY,
Vice Presidents

FILING OF ABSTRACTS AND CASE-RECORDS

SIR,—In the illustration of the card for the filing of extracts which Mr Duncan and others use at the Hillingdon County Hospital (Sept. 22, p 370) it will be noticed that the corner of the card is not snipped. Snipping is essential in all punch-card methods so that the card is filed neither upside-down nor back to-front which would spoil extraction

There are one or two suggestions I would like to offer so far as the layout of the card is concerned If the alphabet, the five vowels and Y, and the figures 5 to 13 be printed along one edge it is possible to use a code which is in use by a large business firm for the primary coding of their customers—namely, the first letter of the word, the first vowel and the total number of letters in the word Thus 'Pentothal' would be coded as Pe9 Using three needles, the number of cards which would fall out, apart from pentothal, will be found to be so small as to be immaterial

Again, instead of numbering the holes from 1 to 31, if they were numbered in three blocks of nine digits *and the cipher, then with three needles this would give* 999 selections instead of 31, and with the spare hole on that side if lettered M would give 1999 To extract units from tens or hundreds the ciphers in the tens or hundreds blocks must be cut; thus 005 extracts 5 from 055 and 505 Taking advantage of the possibilities of combinations and a few needles the items which can be coded in this way are for all practical purposes infinite

I experimented with this method some years ago, and, though it is very dramatic, *I think that for the filing* of extracts the Numerical Alphabetical System supplied by more than one firm is to be preferred The pages are simply removed from the journals and filed in the appropriate folder This means the mutilation of journals but that is unavoidable when one prefers one's office to be a workshop rather than a museum

As for the method recommended for case-records, I would suggest that with the great probability of Whitehall taking an interest in the case-records of all hospitals, any hospital wishing to embark on modern methods will be well advised to get in touch with the work which is being carried out under the Nuffield Trust The "specimen reference code" given in the article cannot be regarded as any improvement on that of the Medical Research Council, which is bad enough

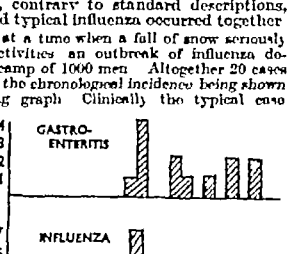
Halifax

A GARVIE

"GASTRIC INFLUENZA"

SIR,—The following account may be relevant to the annotation in your issue of Sept 15 It describes a small epidemic in which, contrary to standard descriptions, gastro-intestinal and typical influenza occurred together

In January, 1945 at a time when a full of snow seriously inhibited outdoor activities an outbreak of influenza developed in a hutted camp of 1000 men Altogether 20 cases occurred in 18 days, *the chronological incidence being shown* in the accompanying graph Clinically the typical case showed a temperature of 102° to 104° F, with headache, backache tracheitis, and sometimes transient vomiting and one or two loose stools



Ten days after the first case cases of apparent gastro enteritis began to report; 13 cases occurred in 14 days the chronological incidence being again shown on the graph. *Clinically* the typical case showed diarrhoea of four to eight motions daily, abdominal pain vomiting at the outset mild constitutional symptoms, and a temperature not above 99–100° F Cultures of stools were not done but the likelihood of the disease being a coincidental bacterial infection was remote for the following reasons: (1) the average outside temperature was consistently below freezing point; (2) another unit in the immediate vicinity, sharing water and to some extent food supply (though not cookhouses) was protected except for a few sporadic cases by the quarantine measures imposed (i.e., closure of cinema and canteens); (3) the periodicity of the case incidence which showed definite peaks separated by 2–3 day intervals suggested a case-to-case infection rather than a food or water borne one In addition there was positive evidence that the two types of illness were the same disease In the first place the successive waves of infection, as can be seen in the graph, corresponded closely for the two conditions In the second place all the gastro intestinal cases were nursed in the same hut as the typical influenzas but none developed any further symptoms

It was difficult on this occasion to regard gastro-intestinal influenza as anything but a different manifestation of typical influenza, and it would be interesting to see reports from other unit medical officers on similar outbreaks

South Wales

J C RYLE

NATIONAL HEART HOSPITAL

SIR,—In the section of your Students Guide (August 25) dealing with postgraduate opportunities I noticed that under Heart and Lungs (p 255) no mention was made of the facilities at the National Heart Hospital where clinical teaching and special courses have continued during the war years

The hospital is planning to extend its programme of postgraduate teaching during the coming year and students wishing to attend should communicate with the secretary Special courses will be arranged and advertised as previously and certain of these will be reserved for medical men demobilized from the Forces

National Hospital for Diseases of the Heart Westmoreland Street London W1

B T PARSONS-SMITH
Dean of the Medical

GASTRIC CANCER AND PERNICIOUS ANÆMIA

SIR,—I was very interested in your leading article of Sept 29, and agree with you concerning the difficulty in early diagnosis of gastric cancer as a complication of pernicious anæmia I should like to bring forward the use of the sedimentation-rate, corrected for anæmia, as a possible aid in some cases

In 1936 I reported (*N Z. med J* 1936, 25, 310) a considerable amount of work on the blood-sedimentation rate in different conditions At that time I used the sedimentation-rate by Wintrobe's method in the routine follow-up of all my cases of pernicious anæmia I found in one man, who had suffered from pernicious anæmia for five years and was being treated with stomach extract, that the usual dose of extract was insufficient to maintain his blood at an adequate level. His corrected sedimentation-rate was slightly above normal, but he had no clinical evidence of complicating disease. Six months later he returned with a greatly increased sedimentation-rate and an inoperable carcinoma was discovered Following this occurrence an X-ray examination of the stomach was made on all pernicious anæmia patients who had even a slightly raised corrected sedimentation-rate but had no obvious clinical signs to account for the increased rate By this means I discovered two more patients who had developed gastric carcinoma, both fortunately were in the operable stage

I realise, of course, that some cases of early gastric carcinoma do not cause an increased corrected blood-sedimentation rate, but the test is so simple that it might well be added to the routine follow-up of patients with pernicious anæmia.

C J C BRITTON.

Bland-Sutton Institute of Pathology, Middlesex Hospital

ARTIFICIAL RESPIRATION

SIR,—I am grateful to Mr. Eardley Holland for pointing out (March 10, p 324) that he had known and successfully adopted the method of artificial respiration by rib traction long before I described it I am glad to note that he prefers it to Silvester's method for resuscitation on the operation table I can, however, assure him that I had never heard or read of this method before I wrote about it (Feb 24) The idea came to me when I was making a study of the individual rôle of the intercostal muscles and diaphragm in respiratory movements So far as I am concerned it was a new idea Now that I find it was previously known to others, I consider it justifiable to call it a rediscovery.

Moradabad, India R. VISWANATHAN.

PREFRONTAL LEUCOTOMY

SIR,—Berliner and others in their article of Sept 15 specially stress the "importance of expert postoperative reablement." I have had the opportunity of comparing some of their results with those that have been obtained when postoperative reablement was necessarily curtailed through war-time shortage of staff The impression I gained was that intensive and sustained re-education contributed greatly to the therapeutic effect of the operation Presumably nobody regards the operation as sufficient in itself, especially in chronic schizophrenics and severe obsessionals; yet postoperative measures are often tackled in rather a cavalier fashion. The mere transfer to a "good" ward is sometimes the limit of assistance afforded to the patient in his task of discarding the habitual psychotic reactions of years and of grappling with reality. he is more or less left to sink or swim That so many achieve some success proves the efficacy of prefrontal leucotomy, but Berliner has shown that better results are possible with sufficient individual care and attention It may not always be feasible, for practical reasons, to give leucotomy patients all the supervision they require, but it should be recognised that the task of the operation is to break the deadlock of an unresponsive personality and make it amenable to reablement · by itself it is only a half measure

There is some evidence suggesting that self-awareness is the complex product of influences arising both in the cortex and in the thalamus. Le Gros Clark, in a recent paper in *New Biology I* (Penguin Books, London) on the basis of sensory experience, suggests that the basal ganglia are "associated with the phenomenon of subjectivisation" and the idea of the self It is of interest that bilateral lesions in the prefrontal region tend to reduce self-consciousness and cause indifference to the opinion of others and to the quality of social conduct Severance of thalamoprefrontal fibres by leucotomy may thus lead to an alteration in self-awareness, and this not only lessens the conflict and tension engendered by outside influences, but also paves the way for educative measures.

Netherne Hospital, Coulsdon F. KRAUPL.

LIVER BIOPSY

SIR,—The history of liver biopsy by means of a trocar in man is considerably older than is generally realised. What I believe to be the first record of this procedure is communicated in F. T Frerichs's monograph *Über den Diabetes*, Berlin, 1884 (foreword dated Sept. 2, 1883), on p. 272, and the biopsies were performed by none other than Paul Ehrlich who was then working in Frerichs's clinic in the Charité Hospital.

They were done in the course of investigations into the question of increased glycogenesis in diabetes. Table III of the work mentioned has seven chromolithographs of drawings of the obtained liver tissue, stained for glycogen with iodine gum-arabic, a method which Ehrlich had described in a paper Über das Vorkommen von Glykogen im diabetischen und normalen Organismus, published as appendix to an article by Frerichs Über den plötzlichen Tod und das Coma bei Diabetes (*Z. klin. Med.* 1883, 6, 33). In one diabetic there was almost complete absence of glycogen; while in a second case glycogen was diminished and irregularly arranged, and showed in parts changes in staining properties which led Ehrlich to assume that it was at these sites bound to some other substance A normal control case showed abundant glycogen

Regarding Dr Sherlock's paper on aspiration liver biopsy in your issue of Sept 29, it would be helpful to learn, for assessing the place of biopsy in diagnosis, in how many of her 264 cases a diagnosis could not be reached with confidence by other means, and in how many cases a previous diagnosis had to be abandoned because of the histological evidence Her warning that if in cases of acute hepatitis "biopsy is postponed until convalescence, normal liver tissue may be observed, and diagnosis is then impossible" is perhaps a little startling to those who have made this diagnosis without a biopsy And in cases of suspected malignancy of the liver, would not peritoneoscopy offer a still smaller risk than aspiration biopsy, as well as a greater chance of obtaining a satisfactory answer?

St Mary Islington (LCC) Hospital, Highgate Hill, London, N19 HERBERT LEVY

BOOKS AND JOURNALS FOR POLAND

SIR,—The council of the Polish Medical Association in the British Empire has decided to appeal to the British medical world for books, textbooks, and periodicals which are urgently needed in Poland

You may know that during the German occupation not only were no new books published but also the existing libraries were robbed and most valuable books confiscated. The final stage of war has practically completed the destruction

At the present moment great efforts are being made to train young people for the work of reconstruction The greatest difficulty encountered in this task arises from the lack of books and textbooks Professors and teachers, who were unable to keep in step with the progress made in all the fields of science during the past six years of war, lack even old textbooks, and reference books, not to mention new scientific publications. In the field of medicine, which is our Association's main concern, the need is so dire that we feel justified in asking help

The books can be in either English, French, or German. Volumes of *The Lancet*, the *British Medical Journal*, *Nature*, the *Medical Officer*, &c, would provide university libraries with material indispensable for the work both of students and professors

B JEDLEWSKI,
President, Polish Medical Association in the British Empire

*** We shall be happy to forward to the Polish Medical Association any books or journals sent in response to this appeal, and addressed to us at 7, Adam Street, Adelphi, London, WC2 —ED. L.

Obituary

THOMAS WILSON PARRY

M A, M D CAMB, F S A

DURING a lifetime of enthusiastic research Dr Wilson Parry uncovered some interesting facts about primitive peoples, especially about their custom of trephining the skull In this operation—which was carried out on infants as well as adults—a disk of bone was removed by scraping through the tables of the skull presumably with a sharp flint or bronze instrument Possibly the practice was intended to relieve epilepsy or infantile convulsions—or from the operator s point of view, to release the devil in possession Parry learned that among the natives of New Guinea trephining is still some times undertaken in an attempt to cure intractable headache He published some twenty papers on this strange practice many of which he first delivered as addresses to the North London Medical and Chirurgical Society the history section of the Royal Society of Medicine, the International Congress on Medical History, and other interested bodies.

Elliott & Fry

His father was Joseph Chatwyn Parry who for many years was manager of the Bank of Lucknow, and played a distinguished part in the defence of that city during the Mutiny Thomas Wilson Parry was born in 1860, after the return of the family to England, and was educated at Amersham Hall, near Reading then a well-known nonconformist school, numbering among its alumni such men as Augustine Birrell, Buckston Browne, and Cozens Hardy He went on to St John's College, Cambridge, graduating in the natural sciences tripos in 1887 His clinical training was gained at St George's Hospital where he held several resident appointments. In 1894 he married and started practice at Youlgreave in Derbyshire, but eight years later he moved to Crouch End, where the rest of his professional life was spent.

W L-B writes: "Sympathetic, gentle, and courteous he endeared himself to his patients, and to these qualities was added a fine clinical acumen Devoted as he was to practice, however, it by no means exhausted his activities; his status as an anthropologist secured his election as a fellow of the Society of Antiquaries and he became the leading authority on prehistoric trephining His poetic gifts were both graceful and learned, as is shown in his sonnet sequence *Great Names* and in his fairy poems, which reveal his tender insight into the minds of children. One felt his essential goodness; sincerely religious, he loved whatsoever things are lovely and of good report In 1937 he became seriously incapacitated by ill health against which he struggled so gallantly that he was able to continue some of his literary work It was a great joy to him that in 1942 he was well enough to be able to revisit his beloved university But the improvement did not continue and the end came peacefully on Sept 21 '

Dr Wilson Parry and I ' writes F G L, "entered the wards of St George s Hospital at the same time and clerked for the same physician, and a close friendship between us thus ensued which was unbroken up to his death He was gifted in many directions as well as in medicine He had a happy talent for verse, and was accustomed for many years to send to his friends—and I was a constant recipient—Christmas greetings conveyed in a very delightful sonnet A staunch upholder of the best ethical traditions of the profession he enjoyed a large practice and was much loved by a wide circle of patients He was especially fortunate in his family life and was greatly gratified that his two sons elected to adopt medicine as their profession '

He married Miss Sophie Cole, who survives him This sons are Dr Wilson E C Parry, of Holbrook near Ipswich, and Captain S. Chalmers Parry, deputy MOH for Worcestershire, now serving in Germany Their one daughter, to the great grief of her family, died as the result of a bathing accident at the age of 21

RALPH MARSH DE MOWBRAY

F R C S

Mr de Mowbray of Lymington, who died in London on Sept 24, was the son of the Rev J H M de Mowbray and was born at Vinoslington in 1887 Educated at Marlborough from 1901 to 1905, he qualified in 1914 from St Thomas's Hospital, where he was house-surgeon and casualty officer, and took his FRCS in the same year His war service in the RAMC included a year at Netley and 3½ years at a general hospital at Deolali in India where he was surgical specialist and had charge of the surgical division, with the rank of captain Afterwards he settled in general practice at Lymington, in partnership with the late Dr F H Maturin

N M G writes: "It was a commonplace—not only among the many patients grateful for his surgical skill but among his professional colleagues—that Ralph de Mowbray 'ought to have been in Harley Street' His surgical knowledge, craftsmanship application, and attention to detail would certainly have ensured his success there not to speak of his rather sombre good looks, lit up from time to time by his rare but delightful smile, and his 'surgeon's hands' which came up to the *highest standards of the novelist* Yet, as the surgical partner of a large firm ranging widely over the New Forest; with three excellent small hospitals at his command; with his love of horses and other animals, with his four tall sons and his tall house in the High Street with its garden overlooking the Solent and the Isle of Wight, and the workshop where he made and carved his beautiful pieces of furniture, I am sure he lived a happier and fuller life than in London There was perhaps, only one drawback—he never had the time to write and publish the varied and interesting cases that came his way To have survived a coronary thrombosis and got back into full business as the senior partner for some ten years of strenuous practice must be a very rare achievement, and his sudden death at a comparatively early age will be regretted by a host of friends and grateful patients '

WILLIAM MARCUS KILLEN

B A, M D, M CH BAI

THE death of Dr Killen on Sept 1 breaks almost the *last link between the present clinical teachers of the* Belfast medical school and those of the nineteenth century

Born in 1863, he was the son of the Very Rev T Y Killen, DD at that time a leading divine in the Irish Presbyterian Church From the Royal Academical Institution, Belfast he entered the Queen's College Belfast, and in 1884 graduated in arts with first-class honours, gaining also the senior scholarship in natural history Three years later he took the degrees of MB MCh&MAO in the Royal University of Ireland After a period of study at the London Hospital in Dublin and in Vienna he was appointed in 1892 assistant surgeon to the Belfast Ulster Eye, Ear, & Throat Hospital Belfast It was in this hospital that the late W H McKeown introduced the practice of early operation on immature cataracts and the use of a magnet for removal of metallic foreign bodies from the eye On the death of McKeown in 1904 Killen became senior surgeon, a post he held until his resignation in 1934 having served the institution for 42 years. During the war of 1914–18 he carried on its work almost single-handed

Quiet and unassuming by nature, and happiest in his clinical and teaching work he did not seek position or honours, but in 1912 his colleagues in Belfast persuaded him to accept the chairmanship of the Belfast division of the British Medical Association and his outstanding work in his special subject led to his election to the presidency of the Irish Ophthalmological Society and vice-presidency of the section of ophthalmology of the BMA

' Dr Killen,' writes a colleague was a great conversationalist One of his greatest pleasures was to welcome any of his large circle of friends to his hospit

able fireside, where, in the happy interchange of talk, time was forgotten Descended from generations of clergy, he retained throughout his life an intense interest in theological problems, and sooner or later the conversation turned to such subjects as the rival doctrines of free will and predestination, or the reconciliation of religious faith with scientific principles, and other kindred questions Although brought up in a strict calvinistic atmosphere (where even the singing of hymns and the introduction of instrumental music into the church service were viewed with dislike and suspicion) he was the most liberal-minded of men. he always studied both sides of a question and respected the other man's outlook, like Montaigne he believed that often 'to know all is to forgive all' He was also very generous, no deserving charity was refused, private patients in difficult circumstances were treated free, and hospital patients sometimes became pensioners from his purse. Although he reached a patriarchal age, William Marcus Killen died young, with his intellect clear and his mind elastic and receptive, and still retaining the affectionate regard of former patients, students, and colleagues"

ARCHIBALD PENRHYN BOWDLER

OBE, M A, M B CAMB

Dr A P Bowdler, who died on Sept 26 at Bournemouth, was one of the small band of pioneers who formed the nucleus of the RAF medical service, and his colleagues of those early days recall gratefully his sane and helpful contributions to the discussions on its numerous problems "In those days," writes C B H, "we needed men who would work unsparingly, men who could overcome difficulties, and, above all, men of good temper and genuine medical knowledge Bowdler had all these attributes in generous measure It was by securing people of his type at the beginning that the RAF medical service later drew so many good men to the ranks of the permanent establishment"

Archibald Penrhyn Bowdler took a second-class in the natural sciences tripos in 1898, qualifying at St Thomas's Hospital three years later and taking his MB Camb. in 1902. He held clinical assistantships in the throat and ear departments of St Thomas's Hospital, and continued his medical studies in Paris where he was for a time resident medical officer at the Hertford British Hospital During the last war in his work on the Central Medical Board of the Air Force he developed between the members of the board and the candidates or sick pilots a personal relationship such as exists between the best type of general practitioner and his patient With the rank of lieut -colonel RAF he continued this side of his work as president of the Aviation Candidates Medical Board His observations on defects of visual acuity among accepted candidates and experienced pilots were published in the *British Journal of Ophthalmology* in 1920, and he contributed to the Medical Research Council report on the medical problems of flying an able chapter on the selection of candidates, which was based on a comparison of the cardiovascular and neuromuscular systems of successful pilots and unsuccessful pupils Before his retirement to Bournemouth Dr Bowdler lived for many years at Chiswick

RICHARD TRAVERS SMITH

M D DUBL., F R C P I

Dr Richard Travers Smith, consulting physician to the West Middlesex Hospital and psychotherapist to the West End Hospital for Nervous Diseases, died at his home in London on Sept 28 at the age of 73 The second son of John Chaloner Smith of Bray, co Dublin, he was educated at Strangeways School and Trinity College, Dublin, where he graduated in medicine in 1894. Two years later he took his MD, and after postgraduate study in Vienna he returned to practice in Dublin He was appointed physician to the Richmond, Whitworth, and Hardwicke Hospitals, and later became professor of materia medica and therapeutics at the school of the Royal College of Surgeons in Ireland In 1899 he was elected to the fellowship of the Royal College of Physicians of Ireland and became a censor and examiner of the college In 1915 he left Ireland to join the RAMC and served with the rank of major at Colchester Military Hospital and as officer in charge of the medical division at the Royal Herbert Hospital, Woolwich. After demobilisation Dr Travers Smith settled in practice as a consulting physician in London and was appointed to the staff of the Miller General Hospital, Greenwich, and of the West Middlesex Hospital After a few years he became deeply interested in psychotherapy, and on retirement from the Miller Hospital he gave most of his time to this branch of medicine, later joining the staff of the West End Hospital Although he accepted Freudian principles he identified himself with no particular school, and his method consisted of detailed anamnesis, explanation, and persuasion One of the original members of the Association of Physicians, his work in his new specialty was based on his sound knowledge and wide experience of general medicine, and his published work reflect his interest in the psychological aspects of cardiology. During the war of 1939–45 he served as a psychotherapist with the EMS

"You could not wish for a more charming and helpful colleague than Dick Travers Smith," writes C W D. "His good humour and ready wit endeared him to all, and his stock of humorous Irish stories was inexhaustible For his patients he spared himself no effort, and they valued his sympathy and understanding Though some deplored his comparative desertion of internal medicine, psychological medicine gained by it, and he died as he would have wished, in full harness, working up to the last day"

JOHN WOOD

M B ABERD, D T M

THE sudden unexpected death of Dr. Wood, from coronary thrombosis, will be deeply regretted by friends and colleagues at Bournemouth and elsewhere.

Born in Aberdeen in 1890, he was educated at Gordon's College and at Aberdeen University where he qualified in 1912, at the age of 22 From the first, his intention was to enter the foreign mission field, and after a house-appointment he took the DTM at Liverpool in 1915 in preparation for work under the ægis of the Church of Scotland After ordination, he was directed to Calabar, in Southern Nigeria, where he had charge of the Mary Slessor Hospital at Ztu and of eleven widely scattered mission stations based on it After some time there, he was transferred to a newly built hospital and mission station at Uburu Being young, keen, active and conscientious, he speedily mastered the local dialects and made his work indispensable But his health and his wife's health suffered so severely that both were ordered permanently home On his return, he settled in practice at Wigan, being appointed assistant surgeon to the Royal Infirmary. But after five strenuous years, again for health reasons, he moved to Bournemouth where he continued to work until his death

"In all he did," writes S. W S, "John Wood seemed to be guided by an abiding faith to support in him a matchless fortitude and determination in a nature both kind and gentle Constantly, in all manner of ways, he strove to do good and to help and encourage others, with never a thought of self There was in him all the fine qualities of the stock from which he came all the virtues went to build in him that nobility of character we knew to be his Near the surface, often breaking out unexpectedly, lay a quiet, pawky, dry humour that was characteristically Scottish He possessed the quiet, tranquil mind along with a becoming humility, owning all the attractive attributes with which Newman endowed the true gentleman. It has been well said that what counts most in living is not so much what a man does as what he is Of all men, John Wood could claim to say, 'I have fought the good fight, I have finished the course, I have kept the faith'"

Dr. Wood's wife survives him, with their family of five children.

ROYAL SANITARY INSTITUTE —Today, Saturday, Oct 13, at the Hope Hospital Annexe, Eccles Old Road, Salford, 6, Dr J L Burn will read a paper on new remedies in disinfestation On Wednesday, the 17th, at 2 30 P.M, at 90, Buckingham Palace Road, London, SW1, Lieut -Colonel M H Webster, RAMC, will speak on uses of DDT in the field

On Active Service

CASUALTIES

KILLED

Captain PETER HAMILTON BARKER M B GLASG., RAMC
Captain JACOB HYMAN JOSEPH M B WALES RAMC

DIED

Colonel MAURICE BAYLIS KING MC, M D DUBL RAMC

AWARDS

MENTIONED IN DESPATCHES

RAMC—
Colonel J P MACNAMARA
Lieut.-Colonels—H. J CROOT
C L. HAY-SHUNKER, J F HEELOP R C. LANGFORD
J R. OWEN, J M. MCINTOSH
Majors—G W GRIG G T
ABELEY, J BROWN J M.
CLOW MBE, J O COLLIN,
T E. HENDERSON, E. L O
HOOD O. H. HOSKYN G J O
KEYS J D MACCALLUM,
W O CALLAGHAN W H.
WOLSTENHOLME T K.
HOWAT the late R STUPPELL
Captains—G M ABRAHAM
N C. BURNLEY-JONES M.
CATURANI, R. G FORREST
J B. GREAT REX J K.
HAMPSHIRE, J HARRIS T B
HARRISON M H. HUGHES
G KILDOUR, H. A. KRIEBER
J K. H. MCCULLOUGH, P H
NANKIVELL, B RADO J H.
REES, R W TIBBETTS,
W T WALKER, G L. WHITMORE J M. MCLEAN J A.
MCPHERSON

IAMC—
Lieut Colonels—T.J DAVIDSON
V D GORDON W MCN
NIBLOCK A. E STEVENS
Majors—A C TEMPLETON
L. M. KELLY MBE, M K.
KRISHNAMURTI R I KRISHNASWAMY G B R. WALKEY
J G WEBB
Captains—B R. ISAAC K. S
GREWAL, K B R RAO
L. N BUDHRAJA, MBE N N
NARAYEN NURUDDIN PARGAT SINGH P C NEDUNGADI
SRINIVAS RANGANATHAN
Lieutenants—DHIMAN BARUA
PRANDAR GOGOI R J
CHANDRA

IAMC—
Major J EDWARDS
Captains—B G KIDDLE MC
M P MCMURRAY MOHD
IMAMUDDAFAR, R. P BHATIA
Lieutenants—ABDUR RASHID
C M. PATNAIK, O P TREHON

INFECTIOUS DISEASE IN ENGLAND AND WALES

WEEK ENDED SEPT 29

Notifications—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1509; whooping-cough, 920; diphtheria 486, paratyphoid, 11; typhoid, 15; measles (excluding rubella), 406; pneumonia (primary or influenza), 802; puerperal pyrexia, 124; cerebrospinal fever, 17, poliomyelitis, 40; polio-encephalitis, 1 encephalitis lethargica, 0, dysentery, 261; ophthalmia neonatorum, 66 No case of cholera or typhus was notified during the week.

The number of service and civilian sick in the Infectious Hospitals of the London County Council on Sept 28 was 1060 During the previous week the following cases were admitted: scarlet fever 65; diphtheria, 45; measles, 0 whooping-cough 21

Deaths—In 126 great towns there were no deaths from enteric fever, measles, or scarlet fever, 5 (1) from whooping-cough, 6 (2) from diphtheria, 75 (6) from diarrhœa and enteritis under two years, and 8 (0) from influenza The figures in parentheses are those for London itself

Liverpool reported 14 deaths from diarrhœa and enteritis

The number of stillbirths notified during the week was 303 (corresponding to a rate of 30 per thousand total births), including 19 in London

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DR B S PLATT will represent the Medical Research Council in the United Kingdom delegation to the United Nations Congress on Food and Agriculture which opens at Quebec on Oct 16

MAUDSLEY HOSPITAL.—As the Maudsley Hospital is the only centre for training in psychiatry in England the mental hospitals committee of the London County Council propose to add temporarily to its establishment eight positions of senior registrar to be filled by doctors released from the Forces who wish to become specialists and consultants in psychiatry Those appointed will fall into class III in the Ministry of Health's scheme of postgraduate education, and their salaries (£550 a year plus board and lodging or an allowance of £100) will be recovered by the LCC from the Ministry The hospital was reopened to inpatients at the beginning of last month Dr A B Stokes has been appointed medical superintendent "on a temporary basis subject to a review at any time"

Notes and News

DEMOBILISATION OF UNITED STATES ARMY DOCTORS

A REVISED point system will return 13,000 doctors 25,000 nurses, and 3500 dentists to civilian life from the US Army by the end of the year Those medical and dental officers who have 80 points are 48 years of age or have been in the Army since before Pearl Harbour will be released as surplus officers unless they are specialists in ophthalmology otolaryngology, plastic surgery, orthopædic surgery, or neuropsychiatry, or are laboratory technicians These specialists will be released if they were called to active duty before Jan 1, 1941 This is described as a drastic lowering of points below the previous plan which was based on an adjusted service score of 100 for non-scarce Medical Corps officers and 120 for those in scarce categories In some cases essential officers may be retained until replacements are shifted to their positions, but none will be held in service after Dec 15, 1945, without their consent

It is anticipated that on the basis of an army of 2½ million a total of 30,000 doctors 40 000 nurses, and 10,000 dentists will be released by next July, and if the armies of occupation and troops in the United States are concentrated at large posts these figures will be exceeded They represent approximately 70% of the peak strengths of these corps at VE-day

POLISH UP YOUR POLISH

THIS war has taught British doctors, if nobody else that it does not do to take one's stand on the English tongue and leave the other fellow to learn it England has been a polyglot community for several years now An ingenious pocket book[1] by Dr W Tomaszewski, just published, contains a Polish vocabulary of about 3000 mainly medical terms a list of 66 genetical and cytological terms; about 140 prefixes and suffixes commonly found in medical words another 24 found in chemical verbal compounds; 232 (mostly uncommon) abbreviations; a list of English abbreviations of degrees, diplomas, and appointments; a useful comparative table of the three main scales of thermometry; weights and measures remarks on prescriptions; a list of medical schools and licensing corporations in Great Britain and Ireland 42 bedside phrases for use with patients; 7 plates of illustrations of medical and surgical instruments and apparatus and 4 blank pages for notes. The bedside section, however is scanty compared with the phrase books issued by the League of Red Cross Societies—subject of a recent annotation (*Lancet* 1945 ii, 214) Dr Tomaszewski's bibliography includes two titles which should be noted by the student of polyglot medicine: A Biraud's *Polyglot Glossary of Communicable Diseases* (*Bull Hlth Org LoN* 1943–44 10 201) and J S F Mario's *English, German French, Italian Spanish Medical Vocabulary and Phrases* (Philadelphia 1939)

USE OF DDT

A BULLETIN issued to the US Army from the Surgeon General's office in Washington describes the precautions to be taken in handling DDT, its mode of action in insect control, and the methods of application

It is emphasised that although DDT may be safely handled as an insecticide it is nevertheless a toxic material Poisoning may follow from ingestion, or absorption of solutions through the skin DDT powder and aerosols are not absorbed through the skin, and have been found to have no [illegible] when inhaled in small amounts But where air [illegible] do not carry the dust away from the user, it is wise to wear suitable respirators

DDT acts on insects both as a contact poison and as a stomach poison Its effect on mosquito larvæ is [illegible] powerful as that on the adult but with some other insects, such as flies the larvæ are not equally affected In [illegible] DDT as a mosquito larvicide to open water receptacles [illegible] continued effect may be obtained through the residual action of the chemical but in ponds and streams the effect is much shorter because of the binding action of soil Amounts of DDT greater than 0·2 lb per acre may prove fatal to fish and [illegible] life

One of the most valuable characteristics of DDT is its tendency to remain deadly to insects over a long period applying solutions to walls and other large surfaces [illegible] coarse spray is usually economical, but in applying it [illegible]

1 *Short Anglo Polish Medical Dictionary* London [illegible] 6s 6d

or mesh surfaces, brushes may be used Although the treated areas remain effective for some time, the insects coming in contact with the chemical may not die for an hour or more

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on Oct. 6, with Mr. Eardley Holland, the president, in the chair, the following were admitted to the membership

T S M Barnett Alexander Buchan, Daphne W C Chun, Aileen M. Dickins, E D Y Grasby, M W Hemans, Ursula M Lister, Agnes M D Milne, Abd El-Salem M El-Minabbawy, Kripananda Mitra, Joan P Molgnard, Padma Raj, W B Shute, Beatrice M Smyth, J M Thomson

Return to Practice

The Central Medical War Committee announces that the following have resumed civilian practice

Mr T A CLARKE FRCS, Ersham Lodge, New Dover Road, Canterbury
Dr L H HOWELLS, 71, Cathedral Road, Cardiff
Dr THOMAS HUNT, FRCP, 49, Wimpole Street, London, W1
Mr H VERNON INGRAM, Ferndale, Clayton Road, Newcastle-upon-Tyne 2 (as from Oct 29)
Mr. B W RYCROFT, OBE, MD, FRCS, 149, Harley Street, W1
Dr J D SIMPSON, 69, Bridge Street, Cambridge
Mr ARTHUR S WESSON, FRCP, FRCS, University College Hospital, Gower Street, London, WC1
Sir RUSSELL WILKINSON, KCVO, MRCS, 82, Portland Place, W1

Future of Physiotherapy

Mr Aneurin Bevan, Minister of Health, will take the chair at a meeting to be held at 3 PM on Saturday, Oct 20, at 28, Portland Place, London, W1, when Mr V Zachary Cope, FRCS, president of the Board of Registration of Medical Auxiliaries, will speak on the place of physiotherapy in a coördinated health service Tickets may be obtained from the secretary of the Society of Physiotherapists, 24, South Molton Street, London, W1

Royal Society of Medicine

There will be a general meeting of fellows on Tuesday, Oct 16, at 5 PM. On Oct 19, at 6 PM, Dr. W M. Levitt will give his presidential address to the section of radiology on responsibility for accidents in radiological departments, and on the same day, at 8 PM, Prof F J Browne will deliver his presidential address to the section of obstetrics and gynæcology He is to speak on the obstetric unit and its place in a national maternity service

Royal Institute of Public Health and Hygiene

During the autumn session the following lectures will be delivered at 28, Portland Place, London, W1, on Wednesdays at 3 30 PM. Mr F D Saner, cancer of the breast (Oct 17), Dr A Doyne Bell, responsibility for child health (Oct 24), Major Joseph Minton, eye diseases in the East (Oct 31), Mr R P Osborne, treatment of burns (Nov. 7); Mr. Anthony Green, radiology (Nov. 14), Mr. J C Ainsworth-Davis, urology (Nov 21), and Dr. W W. Payne, diabetes in childhood (Nov 28)

Mechanical Respirators sent to Prague

A number of "iron lungs" were sent by air to Prague in September for use in the poliomyelitis outbreak. At the request of UNRRA, Dr William Gunn, medical superintendent of the North-western (LCC) Hospital, went to Prague to demonstrate their application

Central Midwives Board

Mr A J BENNETT, assistant secretary to the board, has been appointed its secretary and chief executive officer, in succession to Mr Leslie Farrer-Brown, now secretary to the Nuffield Foundation

LCC Housing Scheme

On Tuesday last the housing and public health committee brought before the Council schemes for erecting 3850 dwellings at a cost of about £4,800,000 on a site of 576 acres at Loughton, Essex, and for acquiring 1481 acres for housing purposes at Dagnam Park, Romford, at a cost of £250,000 The plans for Loughton provide for 3358 houses of three to five rooms, 384 two-room flats in two story buildings, and 108 one room bungalows suitable for the aged The dwellings, it is stated, will all be of "a new type" Sites are reserved for five senior and six junior schools, four churches, sixty shops, a cinema, and two refreshment houses, while Loughton Hall will be used as a community centre About 62 acres is to be allocated to light industries, and a third of this will at first be used for the erection of emergency factory-made houses

Faculty of Ophthalmologists

Our last issue contained (p 448) an announcement on the new Faculty of Ophthalmologists The constitution, functions, and management of the Faculty were outlined in a previous statement, published in February, which has now been amended but in general terms remains valid This previous statement, which was summarised in *The Lancet*, appeared in full in the *British Medical Journal* of Feb. 3, 1945, (p 160), and in the February number of the *British Journal of Ophthalmology*

Association of Industrial Medical Officers

The annual general meeting of the Scottish group will be held on Wednesday, Oct 17, at 3 15 PM, in the Institute of Hygiene, University of Glasgow

Royal Society of Tropical Medicine and Hygiene

At 26, Portland Place, London, W1, on Thursday, Oct. 18 at 8 PM, Dr C M Wenyon, FRS, will deliver his presidential address on tropical medicine in war and peace.

METHYL THIOURACIL, for the treatment of thyrotoxicosis can now be obtained from British Drug Houses, Ltd.

CORRIGENDUM —In Dr Day's letter of Oct 6 (p 449), for "cystometry" read "cyrtometry" His address should be the Mundesley Sanatorium

Appointments

BROWN, ANNIE, MB LOND, DCH part-time senior MO to outpatient department, Hospital for Sick Children, Great Ormond Street
*COHN, ERNST, MD BERLIN temp asst MOH for East Ham.
GUN-MUNRO, S D, MB LOND DMO, Windward Islands, British West Indies
MIDDLETON, MARGARET, MB LOND: part-time senior MO to out patient department, Hospital for Sick Children, Great Ormond Street

* Subject to approval of Ministry of Health

London Hospital —The following temporary appointments are announced

DICK, Wing-Commander I L, MD EDIN, FRCSE, first assistant to the accident and orthopædic department
STEAD, Lieut Colonel J R S G, MRCS, first assistant to Mr Souttar and Mr Perry
SHILLINGFORD, J P, MD HARVARD, MB LOND, first assistant to the medical unit
PASSE, E R G, FRCS, DLO, first assistant to the aural department (part-time)

The following factory surgeons have been appointed

GOLDIE, A. M., MB GLASG Coatbridge, Lanark.
KNOX, H N, MRCS Tring, Herts
LAURIE, J C, MB GLASG Glasgow North

Births, Marriages, and Deaths

BIRTHS

COPLANS —On Sept. 28, at Exmouth, the wife of Surgeon Lieut. Commander Robert Coplans, RN—a son.
CUSACK.—On Sept 27, at Newry, Northern Ireland, the wife of Surgeon Commander J. J Cusack, RN—a son.
EASTCOTT —On Sept 25, in London, the wife of Surgeon Lieutenant H H G Eastcott, RNVR—a daughter
GASS —On Sept. 28, in London, the wife of Captain T. Gass, RAMC—a daughter
JACKSON.—On Oct 4, at Twickenham, the wife of Mr J. M. Jackson, FRCSE—a daughter
MORRIS —On Oct 1, in London, the wife of Captain Kenneth Morris, RAMC—a son
PAIN —On Sept 30, at Northampton, the wife of Captain W J L. Pain, RAMC—a daughter.
WEIR —On Sept 27, at Rugby, the wife of Surgeon Lieutenant M M. Weir, RNVR—a daughter
WENYON —On Sept. 30, the wife of Lieut.-Colonel E J M WENYON, RAMC—twin daughters

MARRIAGES

COWAN—ORMROD —On Sept 25, at Edgbaston, Birmingham, Stuart Lawson Cowan, D SC, to Constance Margaret Ormrod, BM
GRYLLS—DUNNE.—On Sept. 28, at Dartmouth, Henry Grylls, captain RAMC, to Johanna Dunne, QAIMNSR
HUTCHISON—NIBLETT —On Sept. 22, at Colombo, J B Hutchison, FRCS, surgeon commander RNVR, of Glasgow, to N E Niblett, QARNNSR.
LANGHAM-HOBART—TERRY THOMAS —On Sept 19, at Cairo, Neville Langham-Hobart, squadron leader, to Jean Mair Terry Thomas, MB, flight-lieutenant.
MUNDIE—CLEMENT —On Sept 15, at Capetown, James H F Mundie, surgeon lieutenant RNVR, to Dorothie Betty Clement
ROBERTS—HAGGER —On Sept. 19, in Karachi, Iain Gunn Roberts MB, to Joan Margaret Hagger, FMRAFNSR

DEATHS

AITCHISON —On Oct 6, at Hunton Bridge King's Langley, Violet Mary Hawthorn Aitchison (née Rendall), MRCS, DMRE.
CHANCE.—On Sept 28, Clifford Cuthbert Chance, MC, MB ABERD
KIDSON —On Oct. 1, at Northwood, Campbell William Kidson, M B BIRM, major RAMC.
LANCASTER.—On Oct. 4, at Lyme Regis, Ernest Le Cronier Lancaster, BM OXFD, JP, formerly of Swansea, aged 83
MOTTRAM —On Oct. 4, at Northwood, James Cecil Mottram, MB LOND

THIOURACIL IN GOITRE

HAROLD COOKSON, M.D., B.SC. BIRM., F.R.C.P.
PHYSICIAN, CORNELIA HOSPITAL, POOLE

SINCE iodine has been used as a preliminary to thyroidectomy, toxic goitre has been treated with most success by surgical removal of a large part of the thyroid gland. Operative mortality has fallen to a low level, especially in expert hands, and control of the disease may be regarded as very satisfactory. Nevertheless, there has been obvious need of a biochemical antidote, more potent and more permanent in its action than iodine, for the excessive secretion of thyroxine, which is here assumed to be the only means by which the thyroid can produce toxæmia. Such an antidote, though it would not deal with the actual cause of the disease, would represent an advance on surgery.

There were early crude attempts along this line with the milk and serum of animals deprived of their thyroids. Later, after the discovery of the thyroid-stimulating hormone of the pituitary, antithyrotropic hormone (Cope 1938) and large doses of ovarian follicular hormone (Spence 1936, Cookson 1936b, Farbman 1944) were used with the object of inhibiting the output of thyrotropin. Both these methods failed, the first perhaps because the material used was of animal and not human origin, and the second because it inhibits the secretion of gonadotropic hormone only (Spence 1936, Jones and MacGregor 1936) and not the activity of the anterior pituitary as a whole. These experiments were based on the hypothesis that in toxic goitre the thyroid is overstimulated by the pituitary, and subsequent work indicates that this assumption was correct. This is not to say that no other factor over operates; there may be others—e.g., increased blood-supply, as in coarctation of the aorta (Cookson 1936a).

In 1941 a new chapter in the biochemistry of the thyroid opened with the discovery that sulphaguanidine could produce very great thyroid enlargement (Mackenzie, Mackenzie, and McCollum 1941), the histological picture being similar to that seen in primary exophthalmic goitre not treated with iodine. At the same time the growth of the animals was retarded and there was other evidence to suggest that thyroid activity was deficient. Experimental production of hyperplastic goitre in rats was also reported soon after by Kennedy (1942), using thiourea, and by Richter and Clisby (1942), using phenylthiocarbamide, a thiourea derivative.

Further work indicated that the goitre was due to increased pituitary activity, that the action of thyroxine on the tissues was not affected (Mackenzie and Mackenzie 1943, Astwood et al 1943), that many other related compounds, of which the most potent and least toxic was thiouracil, had a similar action (Astwood 1943a), and that these substances could neutralise the toxic effects of thyroxine in the human subject (Astwood 1943b, Himsworth 1943, 1944, Williams and Bissell 1943, Bartels 1944, 1945, Nussey 1944, Paschkis 1944, Williams et al 1944, Williams 1944a, 1944b, Reveno 1944, Joll 1944, Rawson et al 1944, Thomson 1944, Palmer 1945, Eaton 1945, Leys 1945a, Williams and Clute 1945, Lenthart 1945). A fuller bibliography is given by Williams (1944b).

Present Investigation

Observations have been made over a period of twenty months on 66 patients with goitre, with the primary object of determining the action of thiouracil in toxic goitre. The diagnosis of toxic goitre is often easy, but sometimes it is difficult, and this difficulty may persist after estimation of the basal metabolic rate (BMR). When a patient has a goitre and symptoms such as tachycardia, tremor, loss of weight, nervousness and even auricular fibrillation it is not always certain that the goitre is responsible for these symptoms, or, if so, to what extent. For this reason the cases were divided into three groups according to whether on clinical grounds the goitre was toxic, probably toxic, or only doubtfully so. In some patients it became evident that the goitre was playing no part in their symptoms, and the results in these thus provided information about the effects of thiouracil in non toxic goitre.

GROUP I.—CLINICALLY TOXIC GOITRE

This group of 33 patients, 31 of whom were women, ranged from 15 to 81 years in age, with an average of 48 (Cookson 1939). The goitre was nodular except in two girls of 15 and 18, in whom it was smooth. All had such classical symptoms that the clinical diagnosis appeared certain. The BMR was taken as the best index of the excess of thyroxine acting on the tissues at any given time. The BMR before treatment with thiouracil ranged from +15% to +75% with an average of +45%. The drug was given in a daily dose of 1 g. (0·2 g. five times a day) in the cases which first came under observation, but the initial dose has since been progressively reduced and is now 0·2 g. three times daily. Fig. 1 shows the initial BMR and later readings after giving thiouracil in 31 cases. With a few exceptions to be mentioned, the BMR begins to fall in 1–2 weeks and has usually reached normal within 6 weeks, though there is a considerable variation in the time required, with extremes of 3–16 weeks. *No close relation between the length of* this period and the severity of the case, nor to previous treatment with iodine, was found.

Within a few days or a week the patient may say she feels better, but it is unusual to get much objective

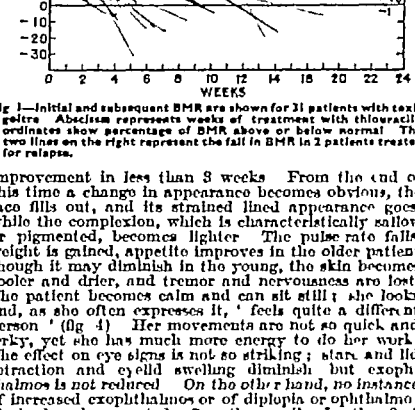


Fig. 1.—Initial and subsequent BMR are shown for 31 patients with toxic goitre. Abscissæ represents weeks of treatment with thiouracil; ordinates show percentage of BMR above or below normal. The two lines on the right represent the fall in BMR in 2 patients treated for relapse.

improvement in less than 3 weeks. From the end of this time a change in appearance becomes obvious, the face fills out, and its strained lined appearance goes, while the complexion, which is characteristically sallow or pigmented, becomes lighter. The pulse rate falls, weight is gained, appetite improves in the older patient though it may diminish in the young, the skin becomes cooler and drier, and tremor and nervousness are lost. The patient becomes calm and can sit still; she looks and, as she often expresses it, 'feels quite a different person' (fig. 4). Her movements are not so quick and jerky, yet she has much more energy to do her work. The effect on eye signs is not so striking; stare and lid retraction and eyelid swelling diminish, but exophthalmos is not reduced. *On the other hand, no instance* of increased exophthalmos or of diplopia or ophthalmoplegia has been noted after thiouracil. In the first weeks no change can be detected in the size or consistence of the thyroid gland.

The general effect in this group of patients was similar to that of a subtotal thyroidectomy, and, though the immediate results are less rapid, a patient is doing her work at an earlier date than if she had undergone a thyroidectomy. About three months is required for normal health and activity to be regained. It was fairly easy to produce myxœdematous symptoms in this group of patients by giving thiouracil 0·6 or 0·8 g. daily after the BMR had reached normal. This was noted in 6 patients. They complained of a feeling of heaviness and tightness of the skin, or said they felt blown up, also of coldness, fatigue and dullness. Their appearance was bloated, the pulse rate slow, fingers puffy (one patient found it impossible to get a ring off her finger) and the BMR has been found as low as −30%. An unduly high level of blood-cholesterol has not been ever been found.

Maintenance.—After the first three or four weeks treatment the dose of thiouracil was reduced, and when the BMR fell to normal it was further reduced. The

dosage adopted in the later cases was 0 2 g three times daily for the first three or four weeks, then 0 2 g once or twice daily until the BMR fell to normal After this a maintenance dose of 0 2 g daily is usually required, though 0 3 g (0 1 g t i d) may have to be given, or 0 1 g daily may be enough In some it was possible to omit the drug, though with two exceptions there has been a recurrence of symptoms within three months When thiouracil was again given the symptoms were rapidly relieved, more quickly than with the initial course of treatment, a BMR of +20 to +30% falling to normal in about a fortnight (fig 1) The two exceptions who have not required any of the drug for more than three months are a woman, aged 30, who has taken none for 19 weeks, and a man, aged 68, who has had none for 8 months Both remain well.

The thyroid gland showed little change in the early weeks and months of treatment The size and consistence of the swelling are difficult to measure objectively, and it was sometimes impossible to confirm the patient's opinion that it had become smaller and softer. Nevertheless, changes so definite as to be beyond doubt were noted when the drug had been taken for some months, the thyroid gland being larger and firmer in some, smaller and softer in a smaller number In one, who took thiouracil on and off for eight months, the drug was omitted at the end of this time because of toxic symptoms Six weeks later her moderate-sized nodular goitre had almost disappeared and there had been no recurrence of thyroid toxæmia The drug was given to one patient with an exceptionally large goitre Her symptoms were relieved and she has returned to work No increase in the size of the goitre, nor any pressure symptoms, have developed, and she does not wish the thyroidectomy which has been advised.

Cardiovascular System—The X-ray appearances of the heart and great vessels have not been affected in the period of observation, except for reduced pulsation The effects on auricular fibrillation are described below Early left ventricular failure, as indicated by triple rhythm, disappeared in two cases after thiouracil and no other form of treatment

Failures—Thiouracil failed to control the disease in five instances

A woman, aged 75, came under treatment almost moribund, with mental symptoms, auricular fibrillation, congestive failure, and a goitre which extended into the thorax for 5 in She died after six days' treatment including thiouracil

Another woman, aged 81, with fibrillation and failure did not respond She had been under her own doctor's observation for three months with regular tachycardia and congestive failure, her movements were quick and manner alert The BMR estimation, postponed until she had been treated for 18 days, as she seemed too ill for a satisfactory test, was +14% No further test was possible Her ventricular rate was well controlled with digitalis, but congestive failure increased and mental symptoms appeared She died eight weeks after coming under observation, during which she received 23 4 g of thiouracil

In a third woman, aged 57, a diagnosis of toxic goitre seemed well established by a nodular goitre, auricular fibrillation, the radiographic appearance of the heart, which showed some prominence of the pulmonary artery but none of the left auricle and no evidence of a primary cardiac lesion The BMR, +45%, and blood-cholesterol, 80 mg per 100 c cm, both supported the diagnosis, but after 17 days of thiouracil the BMR had risen to +47%, blood-cholesterol to 142 mg per 100 c cm Thereafter the BMR fell but could not be reduced below +20%, and the ventricular rate remained high unless digitalis was also given She did not gain any weight She dropped dead three weeks after discharge from hospital, there was no necropsy This case may perhaps be regarded as a partial failure to respond to thiouracil

The remaining two women who did not react favourably to thiouracil were pregnant One, aged 29, seven months pregnant, had taken iodine for 13 months previously, BMR +52%, basal pulse rate 84 per min, blood-cholesterol 95 mg per 100 c cm; after taking thiouracil 0 8 g daily for three weeks, BMR +112% basal pulse rate 88, blood-cholesterol 160 mg per 100 c cm. She did not complain of any symptoms and had gained 3 lb but had developed œdema of the legs A few days later she went into labour prematurely

In the second, an eight-months' pregnant woman aged 32, the BMR rose from +40% to +51% in 44 days, during which she received thiouracil 18 g, the pulse-rate remained about 100, blood-cholesterol rose from 160 mg to 200 mg per 100 c cm Accurate BMR estimations are difficult in late pregnancy, but, disregarding the readings obtained in these two cases, there was no benefit from thiouracil on periods of three and six weeks

GROUP II.—PROBABLY TOXIC GOITRE

There were 22 patients in whom the diagnosis of toxic goitre seemed probable but not certain. Of these, 21 were women, of ages ranging from 10 to 76 years (average 44) BMR ranged from 100% normal to +39%, average +18%. Three had previously had thyroidectomy, which had relieved their symptoms for some years In most of the patients there was subjective and objective improvement after thiouracil, but the results were less striking than in group I (fig 2). The BMR fell slightly or moderately in the course of 3-8 weeks, there was a reduction in pulse-rate, and a gain in weight of a few pounds but not more. In two thiouracil was stopped because of toxic reactions In six the drug had no significant favourable effect

One was a woman aged 76 who for three years had been under observation for diabetes, goitre, and persistent tachycardia of 110 to 120 During 229 days she received 99 g of thiouracil, but the pulse-rate was unaffected, and, although her weight increased by 9 lb, she felt no better. She was too nervous for the BMR test

Two women, aged 40 and 60, with goitre, hypertension, and tachycardia, and a maximal BMR of +19%, lost weight under the treatment, and neither the BMR nor the blood-cholesterol level altered significantly In one, however, the pulse rate fell gradually from 112 to 84 in the course of 12 weeks One woman with auricular fibrillation, wasting, goitre, and normal blood-pressure showed no improvement in six weeks Her BMR remained at +15%

The fifth case was a woman who was kept under observation from the age of 38 to 42 with goitre, tachycardia (104–120), tremor of the hands, and BP 165/95, at the end of this period her BMR was 100% normal, basal pulse-rate 86 After 59 days on 1 g of thiouracil daily, the BMR was unchanged,

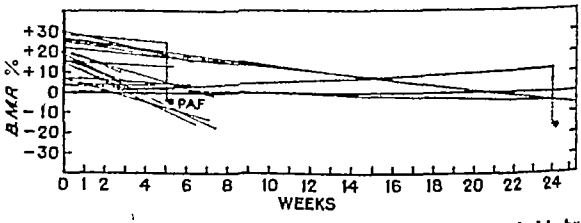


Fig 2—Effects of thiouracil on BMR in 19 patients with probable but not certain toxic goitre Asterisks indicate BMR after thyroidectomy in 2 cases PAF = paroxysm of auricular fibrillation.

basal pulse rate 80, but she had gained 9 lb The drug was continued in reduced dosage till she had completed 208 days' treatment (total thiouracil 96 g), when BMR was +12%, basal pulse-rate 82, but she had gained 11 lb Subtotal thyroidectomy was then done, four weeks later the BMR was −16%, basal pulse rate 86, blood cholesterol 200 mg per 100 c cm. compared with 120 mg per 100 c cm two weeks before operation In the following three months she improved subjectively, feeling and looking much steadier The ambulant pulse-rate was lower, but her weight did not exceed that before operation

The sixth case, a woman of 52, who had a nodular goitre of considerable size, complained of attacks of palpitation, in one attack witnessed the pulse-rate was 180 and regular, but it stopped before an electrocardiogram could be taken Her BMR was +28% before treatment, and +25% after 33 g of thiouracil in 35 days The drug was continued in reduced dose for 397 days (total amount 210 g) She gained 7 lb. but was otherwise unimproved Subtotal thyroidectomy was then done, and 48 hours later there was a paroxysm of auricular fibrillation lasting four hours Three months later BMR was −4%, basal pulse rate 66, and weight 6 lb more than before operation She felt that the operation had improved her health considerably The postoperative fibrillation suggests that excess of thyroxine was still present in spite of the administration of a large quantity of thiouracil

GROUP III—DOUBTFUL TOXIC GOITRE

In this group there were 11 women, aged 22–72 years, average 44, the BMR was within normal limits, ranging from −12% to +18%, with an average of +2·4% In 1 woman it could not be determined because of nervousness The goitre was nodular in 9, smooth in 1, in the remaining case, in which thyroidectomy had previously been done, no thyroid enlargement could be detected

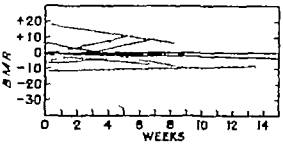


Fig 3.—Effects of thiouracil on BMR in 9 patients with doubtful toxic goitre.

The chief symptoms of tachycardia, nervousness, loss of weight and energy, and tremor were only very doubtfully of goitrous origin Thiouracil (0·6–1·0 g daily) was given for 28–112 days, except in one case, where it was stopped on the 8th day because of malaise and headache In none was there any subjective or objective improvement; weight remained stationary or was lost, there was no consistent reduction in heart rate, and the BMR was unaffected (fig 3) In control periods of observation, when a sedative only was given, there was generally some improvement.

In no patient in groups II and III did the symptoms or signs of myxœdema appear, in spite of prolonged and what would now be regarded as heavy dosage of thiouracil This contrasts strongly with the definitely toxic cases of group I, in which myxœdematous symptoms could be readily brought out with smaller doses in a shorter period

BLOOD CHOLESTEROL

It is generally accepted that in hypothyroidism the blood-cholesterol level rises above normal, but the relation between hyperthyroidism and a low blood cholesterol level is less well established If this relationship could be shown to be close, the blood-cholesterol level might be used as an index of the degree of hyperthyroidism in preference to the more subjective method of BMR estimation

Repeated estimations of blood-cholesterol (using whole blood taken in the fasting state after a BMR test) were made in 52 cases, the results classified as subnormal if under 150 mg per 100 c cm, and normal if between 150 and 250 mg per 100 c.cm (Stokes 1941) There was no instance of hypercholesterolæmia

In group I (cases of definite toxic goitre) 24 patients had low, and 5 normal blood-cholesterol levels before treatment After thiouracil the blood-cholesterol level which had at first been low rose in 19 was unchanged in 2, and fell in 3 In 4 cases with initially low levels there was a rise in 2, no change in 1, and a fall in 1

In group II (probable toxic goitre) the initial blood-cholesterol level was low in 10 normal in 5 After treatment the low values showed a rise in 3, no change in 3, and a fall in 4; with 5 which had been normal 1 rose 1 showed no change and 3 fell

In group III (doubtful toxic goitre) the initial values were 4 low and 4 normal after thiouracil 3 of the subnormals rose 1 fell, and of the normals 1 rose 1 was unchanged, and 2 fell

So far as the results in this small number can be accepted they suggest, when compared with BMR estimations, that in a large majority of clear-cut cases of toxic goitre the blood cholesterol level is low, and that under thiouracil therapy it rises as the BMR falls However, a lag in the changes of blood-cholesterol level was sometimes noted these not being conspicuous till some weeks after a considerable reduction in the BMR. Moreover, there were one or two exceptions in which the inverse relation between blood-cholesterol and BMR was absent In mild or doubtful cases the blood cholesterol levels were on the whole low but showed no uniform changes after thiouracil The results indicate that the blood-cholesterol level bears a close inverse relation to the BMR, but that it is not so close that it can be used as a substitute for BMR estimation in assessing hyperthyroidism.

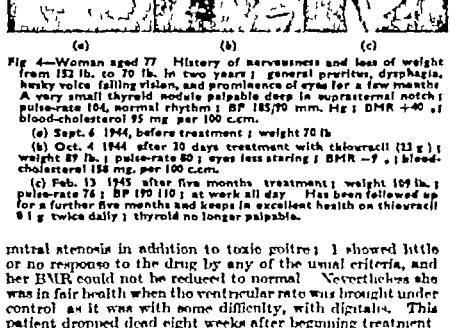
AURICULAR FIBRILLATION

The potency of any measure used to control thyroid secretion can be well tested by its ability to arrest goitrous auricular fibrillation and restore normal rhythm Iodine, for example, will not restore normal rhythm, nor will X-ray therapy, on the other hand thyroidectomy generally does. Dunhill (1937) and Lahey and Hurxthal (1934) restored normal rhythm by thyroidectomy in 80% and 71% respectively; Dunhill's figure including those in which quinidine also was used

Restoration of normal rhythm by thiouracil has been reported by Nussey (1944), Levs (1945a), Melton (1944), Reveno (1944) and Thomson (1944)

In the present series 10 women, aged 43 to 72, had auricular fibrillation In 3 normal rhythm was restored in 3–10 weeks (figs. 5 and 6) In 2 of these the ventricular rate was reduced before the return of sinus rhythm; in the other it was not No digitalis was used at this particular time

Of the 7 in whom thiouracil did not restore normal rhythm 1 was treated for six days only before death; and 1 had



(a) (b) (c)

Fig 4—Woman aged 77 History of nervousness and loss of weight from 152 lb. to 70 lb. in two years; general pruritus, dysphagia, husky voice falling vision, and prominence of eyes for a few months A very small thyroid nodule palpable deep in suprasternal notch; pulse-rate 104, normal rhythm; BP 185/90 mm. Hg; BMR +40; blood-cholesterol 95 mg per 100 c.cm.

(a) Sept. 4 1944, before treatment; weight 70 lb

(b) Oct. 4 1944 after 30 days treatment with thiouracil (1·2 g); weight 87 lb.; pulse-rate 80; eyes less staring; BMR −7; blood-cholesterol 158 mg. per 100 c.cm.

(c) Feb. 13 1945 after five months treatment; weight 109 lb.; pulse-rate 76; BP 170/110; at work all day Has been followed up for a further five months and keeps in excellent health on thiouracil 0·1 g twice daily; thyroid no longer palpable.

mitral stenosis in addition to toxic goitre; 1 showed little or no response to the drug by any of the usual criteria, and her BMR could not be reduced to normal Nevertheless she was in fair health when the ventricular rate was brought under control as it was with some difficulty, with digitalis. This patient dropped dead eight weeks after beginning treatment

Of the remaining 4 1 aged 81 had congestive failure; 1 was stout and apart from the combination of goitre and fibrillation, did not suggest hyperthyroidism and in 2 the BMR was within normal limits

When thiouracil did not restore normal rhythm it was also without effect on the ventricular rate in 5; in the remaining 2 the effect could not be determined because digitalis was given concurrently

TOXIC EFFECTS OF THIOURACIL

Thiouracil shows toxic effects in 10–20% of cases, and no series of cases so far reported has been entirely free from these effects The commonest are skin rashes of various types, adenitis enlargement of submaxillary glands joint pains, headaches, and gastro-intestinal symptoms, including, nausea vomiting, abdominal pain, and diarrhœa A febrile reaction about the eighth day sometimes develops with or without a rash or other symptoms and this suggests a sensitivity state Readministration of the drug after an interval in such cases usually causes an immediate reaction

Jaundice has been reported a few times (Shan and Shorr 1944 Kahn and Stock 1944, Fischkis 1944, Garcill and Lesses 1945) and anæmia (Williams et al 1944). Exophthalmos may increase (Williams and Clute 1945) Heart block has been seen (Morlock 1945) and

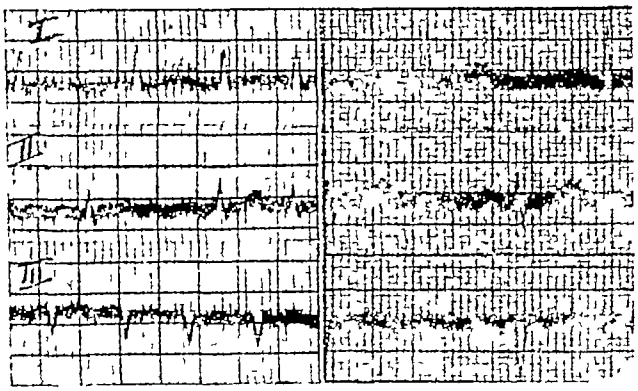
heart-block with pericarditis after methyl thiouracil (Bain 1945)

The intense hyperplasia (Donald and Dunlop 1945) which may develop in the thyroid has raised the question of possible malignant changes, Bielschowsky (1944) has produced a neoplasm in the thyroid of a rat by giving a carcinogenic agent with thiourea

The most serious toxic effect is on the hæmopoietic system, and some cases, a few of them fatal, of granulopenia have been published (Ferrer et al 1945, Gargill and Lesses 1945, Himsworth 1944, Kahn and Stock 1944); 3 of these patients were taking 0 2–0 6 g of thiouracil daily when the fatal complication developed, 1 having had the drug on and off for a year

Fig 5

Fig 6



5 (a) 5 (b)

Fig 5—Woman aged 69, nodular and cystic goitre; first noticed lump in neck 19 years before, main symptom, loss of weight two months; auricular fibrillation, ventricular rate 156 per min, not controlled with digitalis; BMR +35%; blood-cholesterol 80 mg. per 100 c.cm.; after 23 days on thiouracil (18·4 g) BMR +15%, (a) auricular fibrillation, ventricular rate 124 per min, blood-cholesterol 87 mg per 100 c.cm, weight increase 4½ lb, return of normal rhythm on 29th day of treatment; (b) tracing taken 5 days later shows normal rhythm, rate 64 per min After 4 months requires maintenance dose of thiouracil 0 1 g three times daily Feels very well Gain in weight of 14 lb

Fig 6—Woman aged 43; nodular goitre first noticed by the patient 6 months before, symptoms for 4 years, including headaches, loss of weight (70 lb), palpitation, nervousness, and shakiness; on first examination pulse regular, rate 118 per min, BP 160/80; fine tremor, skin warm and moist, still well-nourished; while awaiting admission auricular fibrillation and congestive failure developed; ventricular rate 150 per min, BMR +47%, blood-cholesterol 222 mg per 100 c.cm; 3 weeks' treatment with thiouracil produced little change, and the ventricular rate was still 140 per min.; 2 days before she noted that palpitation had ceased; after 5 weeks' treatment normal rhythm was recorded, rate 78 per min; appearance so much improved that she was hardly recognisable BMR −14%, blood cholesterol 150 mg per 100 c.cm (the fall after thiouracil is unusual), weight gain of 7 lb; well after 16 months' treatment, but stopping treatment for 3 weeks caused relapse with paroxysm of fibrillation. Very susceptible to antithyroid action of thiouracil, the dose of which has to be constantly adjusted to avoid either hypo- or hyper thyroidism.

Various remedies to protect against injury to the marrow have been suggested: thiamine and brewers' yeast by Williams and Clute (1945), folic acid by Goldsmith et al (1944), proteolised liver by Leys (1945b) Pyridoxine hydrochloride intravenously was used by Cantor and Scott (1945) to treat a patient with a granulocytic angina, who recovered. The methyl compound of thiouracil is on trial as possibly a less toxic preparation (Leys 1945a, 1945b), but its superiority is not yet certain It has been suggested that these drugs are more liable to produce toxic effects when there is intercurrent infection, but it may be that in some instances such infections are the result of previous toxic action

In the present investigation there were mild toxic effects in 6 patients (9%) and moderate symptoms in a further 6 (9%) The number of granulocytes was not decreased

Headaches were complained of by 3 patients, but they disappeared when dosage was reduced, or in one instance by substituting methyl thiouracil.

Raised temperature, malaise, and limb pains were noted in 3, the highest temperature recorded being 103° F In 1 of these there was also severe abdominal pain, vomiting, and diarrhœa, yet after an interval she tolerated a second course well Another became sensitised to thiouracil, so that 0 2 g was followed in a few hours by a severe febrile reaction; but she was unaffected by methyl thiouracil Urticarial and morbilliform rashes developed in 3, nausea or vomiting in 3, and articular pains and stiff neck in 3

Unusual cerebral symptoms developed in 1 case, including drowsiness amounting almost to stupor, increased deafness, with headache, and aching under the jaw When tablets of sodium bicarbonate indistinguishable from thiouracil were given, all symptoms disappeared in 48 hours Methyl thiouracil was then given, without the patient's knowledge of the change, and this at first had no ill effects, though after some weeks when having 0 2 g daily, she began to complain of tightness in the neck and upper chest, blurred vision, anorexia, and depression After a further week on 0 1 g daily she felt well This patient had treatment for 11 months, and at the end of this time, in spite of recurrent symptoms for which thiouracil must be blamed, there was no hyperthyroidism and her goitre had almost disappeared.

Of those developing a toxic reaction the drug has been permanently withdrawn in 8—all such mild or doubtful cases that the risk of continued treatment was not considered worth while.

Discussion

The results obtained in this and other published trials indicate that thiouracil can neutralise hypersecretion of thyroxine when tested on cases in which the clinical diagnosis of toxic goitre is beyond doubt In this class there was no instance of its failure, apart from 2 patients in late pregnancy and 2 elderly women with fibrillation and heart-failure, one of them moribund when treatment was begun It may be, however, that the chronic mild toxæmia of a large degenerated thyroid gland cannot be combated, as suggested by 2 patients in group II who improved after subsequent thyroidectomy, 1 of them having a postoperative paroxysm of fibrillation

We are now almost in the position of being able to test the disease against the drug, rather than of testing the drug against the disease That is to say, a secondary use to which thiouracil may be put is as a diagnostic agent in deciding to what extent, if any, symptoms are due to goitre or to other factors, neurosis in particular, though it must be recognised that sometimes an anxiety neurosis is combined with toxic goitre (Rasmussen 1937, Moschcowitz and Bernstein 1944) If symptoms are non-goitrous in origin, thiouracil has no effect and it is usually incapable in ordinary clinical doses of depressing thyroid function, even though it be administered for many months

As the action of thiouracil is still very imperfectly known, rules for its use cannot yet be formulated, but the question of its standing as an alternative to thyroidectomy in the treatment of toxic goitre must arise

The relative merits of the two methods have to be considered in relation to relief of symptoms, risk, aftercare, length of invalidism, and patients' inclination. There are also particular circumstances in which one offers advantages over the other. Thiouracil will control hyperthyroidism as well as thyroidectomy and allow a quicker return to full activity, an ambulant patient need not be admitted to hospital for treatment with the drug.

As for the risk, the case-mortality of thyroidectomy is 0·5%–2% in expert hands, higher in others. These figures mean little, however, unless the type of case is known.

Dunhill (1937) gave his operative mortality at 2·6%, but the proportion of his cases with fibrillation and congestive failure seems to have been large. Lahey and Hurxthal (1934) had a case-mortality of 4·25% in 312 thyrocardiacs; and Hudson (1945) operated on 457 goitres with mild to severe toxæmia without a death, and on 125 with cardiovascular complications with 4 deaths.

Injury to the recurrent laryngeal nerves, tetany, and myxœdema are complications which sometimes, but not often, follow operation.

The risk of fatality in connexion with thiouracil is entirely a question of extreme depression of the leucopoietic system; the case-mortality from this is under 1% in the 600–700 cases so far published. It may be that the risk will be reduced with the smaller doses now used, but it has not been eliminated.

The other and milder toxic effects are distressing, but transient if the drug is stopped or the dose reduced. With a few of them, however, it is prudent to abandon the treatment. In the elderly with cardiovascular complications the risks with thiouracil are no greater than in the young, and here the drug has the advantage over operation. In children also medical treatment has a claim to be used, as it is difficult to balance the amount of thyroid to be left at operation against the needs of growth. On the other hand, with thiouracil the secretion of the thyroid can be readily controlled by varying the dose.

A large goitre is better removed, and this is imperative if there are pressure symptoms. Indeed, any patient who desires to be rid of the swelling in her neck should have operation, although reduction in size or even complete disappearance of the goitre is possible on thiouracil.

The aftercare when symptoms have cleared is much more troublesome both for the patient and her medical attendant, with thiouracil than with surgery, as she has to be kept under supervision for an indefinitely long period. I have had two patients under treatment for 18 months, both still requiring thiouracil 0·2 g. daily, but with adjustment one way or the other from time to time to maintain health.

The drug has also to be considered as a supplement to, besides an alternative to, surgery. Used with iodine in preparation for operation it should be possible to detoxicate patients completely, so that when this course is decided on it will be even safer than in the past. It is a fact, however, that patients in the older age-groups with cardiac complications often go unrecognised for what they are, or are treated with iodine, for too long. In these the disease may be too far advanced for them to be saved by any method.

Summary

Observations on 60 patients have shown that thiouracil is a potent antidote for excessive thyroid secretion, though under certain conditions, which are described, it may fail. It requires several weeks as a rule to restore function to normal.

Hypothyroidism is readily produced in those formerly suffering from hyperthyroidism but extremely difficult or impossible to produce with similar dosage in those with mildly overactive or normally active goitres.

A depressed blood-cholesterol level was found to be fairly closely correlated with a raised BMR, but not so closely that it could be used as a substitute for determination of the BMR.

Observations are reported on the action of thiouracil in auricular fibrillation associated with goitre.

Toxic effects were seen in 18% and are a drawback to the method.

The relative merits and disadvantages of thiouracil and surgery and their use in succession are discussed.

ADDENDUM

Since the above was written, toxic reactions have developed in 3 further patients in the series, bringing the total incidence of these reactions to 23%.

The first, a woman of 65, developed iritis in one eye after 6 weeks' treatment with thiouracil and while taking 0·2 g. daily. Subsequent trial with 0·1 g. of the drug daily, and a third trial of 0·1 g. of methyl thiouracil produced a recurrence of the iritis and rise of temperature within 36 hr. on each occasion. The white cells were normal.

Another woman aged 54, developed painful œdema of the ankles and one hand with granulopenia (polymorph-count 1702). Thiouracil was stopped, and a week later the polymorph count had risen to 3480 per c.mm. During the 3 weeks before the appearance of these symptoms she had taken only 0·2 g. of the drug on five occasions. Before this she had been quite well on 0·1 or 0·2 g. daily for 18 months. The swelling of the ankles, which suggested a periarthritis, persisted for several weeks after thiouracil was stopped, which raises some doubt about whether or not it should be attributed to the drug.

The third patient, a woman aged 44, had likewise been under treatment with an excellent result for 16 months when she developed severe frontal headache. At this time the dose of thiouracil was 0·1 g. t.i.d. Methyl thiouracil 0·2 g. daily was substituted, and the headache disappeared; but she had severe pain in the wrists, slight pyrexia (98·6° F.), and a polymorph-count of 2250 per c.mm. When the drug was stopped, she lost her pains and the polymorph-count rose.

It is evident that a long period of perfect tolerance may be brought to an end by toxic reactions of various kinds, and it follows from this that the incidence of these reactions in any investigation on thiouracil will increase in proportion to the period of observation.

The thiouracil was supplied by British Drug Houses Ltd.

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WOUNDS IN REGION OF HIP-JOINT

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AFTER the invasion of Europe the orthopædic unit at this hospital received a number of casualties with wounds in the region of the hip-joint and with high fractures of the femur Most of these have now been followed sufficiently far for the end-result to be known or forecast with reasonable certainty. We have found the results disappointing and feel that our treatment at the base hospital has been somewhat unsatisfactory.

The object of this paper is to outline the methods used and to suggest improvements Injuries of this type seemed to us to present the greatest difficulties, and a search in the published literature for assistance and advice proved disappointing

In the war of 1914–18 (*Official Medical History of the War*) these cases do not seem to have been looked upon as presenting any very special problem of treatment except that of transport Any form of abduction splinting was found almost impracticable, and the Thomas splint was later used whether or not the wounds were situated in positions convenient for the splint ring The hip was held in a position suitable for ankylosis, which was encouraged and in most cases ultimately took place, and the customary end-result was a stiff hip, more or less short, with one or more discharging sinuses. These seem often to have persisted for years

The *Official Medical History of the War* gives the overall mortality of wounds of the hip as 60%, chiefly accounted for by visceral injuries With British surgeons the problem of drainage does not seem to have loomed very large and, when performed, consisted in the opening of surface abscesses and the curettage of sinuses Attention seems to have been drawn, however, to the importance of removal of the fragmented head of the femur if possible in the early stages

The only reference to the hip found in the *Field Surgery Pocket Book* (1944), issued by the War Office, is that "infection of the hip and shoulder is liable to be overlooked" This scarcely seems to cover the subject

A group of Russian surgeons has recently published papers, reviewed by Aird (1945), indicating a far more radical approach than has previously seemed acceptable in this country Resection of the joint is resorted to in the early stages in those cases where toxæmia does not respond to more conservative measures. Disarticulation at the hip is also often advised

This paper is based on a study of 44 cases treated at this hospital As they have been received here 1–4 weeks after wounding they are necessarily selected Most of such wounds received in the battlefield are complicated by other more serious injuries, which are obviously responsible for the high mortality. Consequently the cases reaching a base hospital are either uncomplicated in this sense, or the complications have been treated and at least partly overcome

Two types of injury are here under consideration: obvious wounds of the hip-joint, and fractures of the neck and peritrochanteric regions of the femur with doubtful penetration of the hip-joint Many of the X-ray films of this latter type show multiple widely scattered foreign bodies and in almost every case severely comminuted fractures The hip may have been affected; but, unless the joint suppurated, its involvement might not have been appreciated.

TREATMENT CARRIED OUT

The primary treatment, apart from first-aid dressing and the application of a Thomas splint, has been almost always within the first 24 hours and in about half the cases within half that time The wounds have been explored and enlarged, any easily accessible foreign body has been removed and in many cases fragments of bone have been unhesitatingly sacrificed

In about two-thirds of the cases a plaster spica was used as the early immobilisation for transport, and in the remainder a Thomas splint The patients were almost all evacuated by air, and at the receiving hospital the first plaster or splint was usually changed and the wound dressed and where necessary, re-explored.

On arrival at this hospital half the patients were, or clearly had been, toxæmic—i e, in 22 cases there has been a more or less lengthy period during which the infection was not under control, in most cases a result of inadequate drainage or immobilisation or both Systemic penicillin and sulphonamides had been used almost as a routine, often with additional local therapy

At the base hospital 26 were treated throughout in plaster spicas, and the remainder had tibial skeletal traction on a Thomas splint as soon as possible with early movements of the knee-joint Delayed suture of wounds was done on 6 occasions only. Sequestrectomies were performed in 10 patients and in 9 of these more than once, 5 major operations for drainage were done of the type advised by Girdlestone (1943), or some modification of it.

RESULTS

In 13 out of 16 cases in which the hip-joint became septic, ankylosis of that joint took place Although in some cases this was not by bone, there was no useful range of movement In 10 the wounds were unhealed at the end of six months In 6 there was an inch or more of shortening

CAUSES OF SLOW HEALING

Inadequate or Delayed Primary Treatment—The difference between delay of more or less than 12 hr does not seem to have been significant in this series, and inadequacy of primary treatment seems a more likely defect. For those with no experience of surgery in forward areas the difficulties in this type of case can only be imagined, and criticism from the base hospital is misplaced. In any circumstances wounds in the region of the hip are among the most difficult to excise efficiently or drain adequately. In a fair proportion of these cases re-exploration, with enlargement of the wounds and drainage of abscesses, was necessary within the first few days, and this fact alone suggests that the primary tre was not effective.

The previous treatment performed on the many thousands of cases passing through this hospital has been of such a uniformly high standard that any remarks about the inadequacy of such treatment are in no sense a reflection on the surgeons concerned The key to early healing of wounds is delayed primary suture, but for this to be successful the primary surgery must have been wholly efficient It seems likely that the difficulties of primary treatment of hip wounds make satisfactory delayed closure less often possible than in other regions

Inadequate Late Treatment—At a later stage we have been slow to appreciate and treat the case that requires only the removal of a foreign body or fragment of dead bone to promote healing of the wound The most difficult cases, however, are those in which an abscess cavity in bone, or surrounded by dense scar tissue, is not being drained and is keeping the whole infective process active Sometimes such a cavity may be situated within the pelvis

One of the patients in this series received a wound of the hip with fractures of the head and neck of the femur and the acetabular floor. At the primary treatment the absence of the head had been noted and the acetabulum was felt to be empty. It had not then been realised that the shattered head had been driven into the pelvis through the floor of the acetabulum

In a second case the head had remained in the socket and the femur had shortened at the fractured neck, the great trochanter riding up towards the ilium The wound did not heal. An excision of the Girdlestone type was done, and the sequestrated fragments of the head were removed, followed by rapid healing of the wound The operation was done 9 months after wounding—9 months of bed, spica, sepsis and ill health It should have been done many weeks earlier

SHORTENING

Shortening is of less importance and is inevitable in many of these cases Where the head of the femur has been destroyed or removed, length must obviously be sacrificed. In the cases without involvement of the head, where the fractures lie in the peritrochanteric region, shortening should not take place It is very liable to do so with increasing coxa vara and outward bowing at or below the trochanters In these instances where ankylosis is not inevitable, we feel that the plaster

plica is an undesirable method of treatment except in the earliest stages and for transport A spica may immobilise and support the soft tissues, but it exercises the same doubtful function on the knee and ankle, and even sometimes on the uninjured joints of the opposite limb

The object of plaster immobilisation in a compound fracture is to promote union of the fracture and to assist healing of the soft parts In transtrochanteric fractures union is not a great problem and here the usefulness of plaster is outweighed by its disadvantages The chief difficulty in these cases is not delay in union but shortening, *and the plaster does not apply and maintain traction effectively*—or, if so, only in the hands of the fortunate few

Pressure sores are only too common under the average spica applied by the average surgeon, particularly in patients emaciated by severe sepsis and in those with anaesthesia from sciatic injuries Moreover, permanent limitation of movement at the knee may preclude operation for the nerve lesion Another danger insufficiently emphasised is that of disturbing the uniting fracture during the changing of the plaster

The difficulties of appreciating uncontrolled sepsis in the wounds are increased when penicillin is being used Unless the area concerned can be easily inspected, these difficulties become almost insuperable On several occasions, also, the diagnosis of intra-abdominal complications has been greatly hindered by the presence of a spica

For all these reasons we feel that the spica, which may be the most satisfactory method when ankylosis of the hip is required, must be, in the other type, looked upon as the last resort and an admission of failure

TREATMENT AND RESULTS OF WOUNDS OF HIP-JOINT

	JOINT INFECTED	JOINT NOT INFECTED	Total
No of cases	21	20	44
Results known	16	11	27
Ankylosed	13		13
Good hip range		10	10
Fair hip range	2	2	4
More than 1 in. short	0		0
Unhealed at 6 months	9	7	16
Treated in spica	19	7	26
Treated in Thomas splint	5	12	17
Delayed suture	2	4	6
Major drainage	5		5
Intrapelvic complications	7	2	9
Sciatic lesions	4	5	9
Toxæmia	13	7	20
Still under treatment	7	8	15

OTHER METHODS OF SPLINTAGE

Apart from the spica and the slung Thomas splint with skeletal traction, three other methods have been used The first is a combination of these two If the ring of a Thomas splint is incorporated in the body of a spica, traction can be satisfactorily maintained, and the ring may be supported by plaster struts to avoid contact with neighbouring wounds. At the same time some degree of immobilisation at the hip can be secured where this is thought necessary We have found this method of splinting useful on several occasions It combines *the advantages of immobilisation with those of traction*, the leg of the spica being replaced by a Thomas splint

The second method used occasionally has been the plaster bed Again traction has been satisfactorily used with this by incorporating a knee-flexion piece at the end both of the bed and of the turning case

Thirdly, the Jones abduction frame has been used, and we have attributed our lack of success with this method to the fact that the frames could seldom be said to fit the patients and that there has been insufficient nursing experience with the apparatus

In the later stages we have found the walking spica useful in cases where it is necessary to hold the hip when ankylosis is desired but is not yet solid

The accompanying table sets out some details of the types of cases and of the results

TREATMENT SUGGESTED

Because there has been comparatively little written on the subject, our methods have been to some extent those of trial and error No lives have been lost, and no limbs have been lost; but it seems that with added experience and knowledge of the difficulties, the morbidity in many cases could have been shortened and possibly lessened As a result of these experiences and these errors we feel that our subsequent treatment of similar injuries will be on the following lines.

Primary Treatment—In many cases the treatment of the wounds and of the damaged bone will necessarily take second place to that of the more serious abdominal and bladder complications and of the associated shock. *Radiography is helpful*, before primary treatment is undertaken, to determine the position of the larger foreign bodies, the nature of the fracture and the degree of comminution, and, if possible, whether the hip is likely to have been involved or not The wounds should be explored and excised in the usual way The larger foreign bodies and, especially, any associated pieces of clothing should be removed if easily accessible Fragments of bone, however loose they may appear, should not be lightly removed, unless they constitute all or part of the head of the femur Some attempt should be made to discover whether the track penetrated the pelvis, and a rectal examination should not be neglected The skin should not be sutured, and the minimum of skin should be excised The primary treatment should conclude with the application of a spica for transport only in those cases in which the joint is or is likely to be involved and in which the position of the wounds makes the use of the Tobruk type of splint inadvisable

Systemic penicillin and sulphonamides should be used for the first four or five days, and all subsequent procedures, *wound closure, removal of plaster, change of* splint, sequestrectomy, and so on, should be performed under a protecting dose of penicillin (Innes and Ellis, 1945) The use of the single "boost" dose or of the short systemic course in these circumstances has been proved over and over again of the greatest importance. On the few occasions when this precaution has been omitted the sort of manipulation above mentioned has usually been followed by a flare of temperature and a temporary deterioration in the patient's general condition.

Definitive Treatment—As soon as the patient reaches the base hospital, the splint or plaster should be removed and the wounds examined A study of the position and condition of these, an estimation of the patient's general condition, and an examination of the X ray films will enable a decision to be reached on the line to be followed If the hip is likely to be infected and ankylosis is the end result in view, plaster immobilisation may continue, but if not it is better replaced by some form of skeletal traction Delayed primary suture should be done if possible

A Steinmann pin through the tibial crest below the tubercle is the most satisfactory way of applying skeletal traction Fixed traction is used at first When the reduction is satisfactory and the local and general infective process is seen to be well under control, sliding traction replaces this and knee movements are started

If the temperature does not settle and the general condition of the patient improve rapidly, the cause should be sought early At this early stage the reason is usually the presence of an undrained pocket surrounding a foreign body, often associated with fragments of cloth

If sinuses persist at a later stage again the reasons should be reviewed at short intervals When a sequestrum is responsible for the continued discharge from such a sinus, its removal is usually followed by rapid healing When, however there is a bone cavity or an area of ill-defined osteitis in cancellous bone, the difficulties are vastly greater Such a cavity will never heal, or at least only after many months unless it is obliterated and the most successful way of doing this seems to be by filling it with purely cancellous chip grafts from the ilium This procedure is very often highly satisfactory, especially under the protection of penicillin.

Intrapelvic or other deep-seated sepsis should be noted early; and, if some radical procedure of the Girdlestone type is required it should be done early rather than late This operation or some modification of it has been done in 5 cases in this series. Although it has been said that it is justifiable only as a life-saving measure, we feel that this view misplaces the emphasis

of its usefulness It may be a life-saving measure, but it is certainly a morbidity-saving one The functional results have been said to be so bad that it should only be used as a last resort. We have not found this to be so—at least in these few cases. Its details should be carefully studied in Girdlestone's original paper (1943) by anyone embarking on the operation.

SUMMARY

On the experience gained from the treatment of 44 cases of compound fractures in and near the hip-joint the following principles are suggested ·

(1) Early treatment of the wound, with removal of large foreign bodies and devitalised tissues, but not of fragments of bone unless these are part of the head of the femur.

(2) Delayed primary or secondary suture of wounds.

(3) Early decision whether ankylosis is either inevitable or desirable.

(4) Treatment in a spica only where ankylosis of the hip is required.

(5) Treatment of other cases in a Thomas splint with skeletal traction.

(6) Investigation of the causes of persistent sinuses under the three headings of foreign body, sequestrum, and undrained cavity.

(7) Early treatment of these causes

(8) Early appreciation of those cases that require radical drainage and the use of the type of operation advised by Girdlestone in this connexion.

The opinions expressed here are those of the orthopædic unit at this hospital under the direction of Mr. V. H Ellis, to whom I am greatly indebted for help and advice. My thanks are also due to the other surgeons under whose immediate care these patients were treated

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MILITARY PSYCHIATRIC CASUALTIES

EXPERIENCE WITH 12,000 CASES

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(*Concluded from p* 457)

Method of Handling

Two sets of machinery are required to deal with the psychiatric casualty one to combat demoralisation and promote rehabilitation; the other to provide specific psychiatric treatment In practice these two processes must be combined, but there may be set-ups which are primarily clinical and others that are primarily military

The evolution of appropriate methods was worked out by Brigadier G W. B James in relation to the 8th Army The machinery then devised has varied in application to different conditions of terrain and strategy and will always need to be elastic to conform with tactical considerations The total set-up requires the administration of five separate processes. filtration, treatment, rehabilitation, reallocation, and evacuation. The organisation is based on the familiar pattern of division, corps, advanced base, and base, and omission of any one of these will be harmful While the efficiency of the psychiatric services will depend more than anything else on the clinical vigilance and psychiatric acumen of the RMO who constitutes the first link in the chain, the psychiatric emphasis will usually fall on the set-up located at the advance base.

ADVANCE FILTRATION UNITS : DIVISIONAL REST CENTRES : CORPS EXHAUSTION CENTRES

The main task for the psychiatrist at this level is diagnostic, there is no time, and the atmosphere and the conditions of work are not suitable, for much that can legitimately be called psychotherapy. The first task is to sort out the men with anguish reactions and those with campaign neuroses and move them without delay to the main filtration centre. The men with panic reactions should be handled as follows:

Allowance is made for a stay of 5 days, during which the man should be given as much sleep as he feels he requires, aided by sedatives Good hot meals, hot showers, and, ideally, a complete change of kit should be provided These centres should be provided on both a divisional and corps basis Documentation should be minimal, and the atmosphere as impersonal and objective as possible until the discharge interview

About 30% of the men treated thus will justifiably be returned to their units; they should be given vigorous but kindly exhortation about the direction in which their future duty lies. The remaining 70%, including the really sick men and those of poor combatant capacity, will then be evacuated to the main filtration centre.

MAIN FILTRATION CENTRE

It is here that much of the specific psychotherapy will be given. This centre will usually be attached to an advanced general hospital Speed of attack, rapid expert assessment, and a dynamic atmosphere which never gives the man cause to feel that "nothing has been done" for him will create the right atmosphere, which is so important in governing the soldier's subsequent reaction to handling. Warmth of personality and compassionate understanding are not incompatible with these.

Men with simple stress reactions who have passed through the forward units will at most be given 48 hours' rest or, if they have already had this, will be passed on immediately to the rehabilitation centre. Anguish reactions require immediate psychiatric treatment This consists of a general attack on dissociative and anxiety features within a total framework of an implied attack on incipient demoralisation Dissociative features, although amenable in some measure to persuasion and suggestion, can with confidence be cleared up by abreaction. I always use ether, and the technique is as follows

Ether Abreaction—A typical instance would be that of a patient complaining of headache, insomnia, mild depression, and general feelings of tension-anxiety, who has returned from the front line as a battle casualty He appeared scared, tremulous, and torpid He may or may not remember spontaneously that his symptoms date from being "blown up." The history is somewhat as follows · he may or may not have been aware of a gradual oncoming loss of grip, and there may or may not have been immediate antecedent circumstances, such as the death of a close comrade, bad news from home, or a "near miss." He often describes himself as having felt that he was in such a tight spot that there was no way out, and he did not expect to survive. Often, in such circumstances, he will have taken cover in a slit-trench and become mildly "jittery", shells are dropping round him, when suddenly he hears an explosion, perhaps sees a flash, and then recalls nothing until he is in a MDS being attended to by the orderlies. An observer would, however, probably fill in the details somewhat as follows after the explosion the man may have gone berserk or may have lain cringing or "jittery" in the slit-trench or apparently stuporose, or he may have simply appeared dazed and only required modified assistance to reach a truck On his arrival at the MDS the symptoms described above assert themselves.

Technique—The patient is placed on a couch, his confidence secured, and full rapport established A full and detailed account of incidents surrounding his loss of memory has meanwhile been obtained It is then explained to him that an explosion can blow not only metal into his flesh but also fear into his mind, and that, until that fear is removed, the symptoms will persist He is persuaded that this procedure is easy and effective, and a brief description of the treatment is given

He is asked to lie on a couch and told that he is going to be given a little ether, during which he must attempt to live over the episode again in his mind, as vividly as if he were watching the whole of the events he has already described being re-enacted on a cinema screen He is then told to close his

eyes, and ether is slowly administered with an open mask, the physician starting him off by saying somewhat as follows: "Now, there you are again in the slit trench. You can see it all perfectly clear again. Who is with you, and what is happening?" Very rapidly he is encouraged and persuaded to begin his tale

After a minute the physician assumes a more dramatic and vivid form of address, a towel is placed on the mask, and in the classic case the patient rapidly changes his narrative fashion from a reflective to a vivid topical mode, as if he were taking part once more in the events on the battlefield He comes to the point where the shell exploded, when he may pass into a state closely resembling that which existed on the battlefield

At this point further research is necessary to determine what is the correct procedure, but on the whole one tends to stop the ether, smartly rouse the patient, and obtain from him details of his subsequent behaviour by a mixture of persuasion and encouragement This need only be done in the barest outline; and, as soon as one has got him to the point which he originally remembered he is rapidly and thoroughly woken up and the whole story recalled to him. Once again what follows requires research to determine the correct procedure In many cases the patient spontaneously bursts into a flood of tears. Where this has not happened an attempt has often been made to induce an emotional reaction, often to the extent of using maudlin suggestion Strong suggestion is then given him that he feels better, and that his symptoms will disappear, and he is sent back to the ward to sleep for a varying period up to 24 hr under sedatives

Narcosis Therapy—The anxiety features are specifically amenable to narcosis, administered as a therapeutic ritual rather than in the form of simple continuous sedation A standard course of 3–5 days is given, consisting of approximately 18 hr sleep out of the 24 hr, but some patients only require 1 day, and some require 10 I consider that the best results are obtained by the use of a barbiturate with paraldehyde Possibly 'sodium amytal' is the barbiturate of choice, but 'Somnifaine' and phenobarbitone are effective The barbiturate is given to maintain a base-line of somnolent quietude, and the paraldehyde is used as a hypnotic to ensure sleep Picrotoxin should always be available, and adequate fluid intake is the best safeguard against complications I have had no fatalities in well over 500 consecutive cases treated During periods of activity I use the treatment in anything up to 20% of my cases, and I regard it as the most valuable single therapeutic agent at our disposal in a forward military psychiatric unit

REHABILITATION CENTRE

Most of the cases will be passed from the main filtration centre direct to a rehabilitation centre, and I do not allow patients to remain in the main filtration centre longer than 10 days, with a statistical average of 5 days

The patients, having passed through the filtration centre, where 35% have been subjected to more or less specific forms of psychiatric treatment, have now arrived at the rehabilitation centre Provision for beds should be made in the proportion of 1 bed at the filtration centre to 5 at the rehabilitation centre, and the psychiatrists available should be divided equally between the two centres.

The rehabilitation centre should provide:

1 A controlled paramedical and paramilitary atmosphere which will discourage the development of invalid reactions but permit the salvaging of missed therapeutic opportunities.

2 A time during which welfare and other problems can be attended to efficiently

3 A regime for the promotion of maximal physical well being which is the basis of all smart military turnout

4 A framework for social rehabilitation during which the tendency of the neurotic soldier to isolate himself can be combated

5 A psychiatric framework which will combat the tendency to valetudinarian self justification.

6 A regime in which the soldier can regain the concept of himself as having a duty to his country, a responsibility to his comrades, and a sense of pride in his profession as a soldier—in short, make him once more into a good soldier with a high sense of honour and duty The motto here is 'discipline, skill morale"

Besides these six basic aims, the rehabilitation centre achieves results which, though not related immediately to the soldier, by themselves justify its creation and maintenance

The following considerations originally prompted the set-up of the first military psychiatric rehabilitation centre in the CMF in February 1944:

1 It acts as an expansible bulb in what may be regarded as a man power pressure circuit, relieving the strain on the filtration centre during a big attack.

2 It acts as a reservoir of treated cases where they can await disposal and avoid the demoralising influence which so often attends the neurotic's stay in holding units

3 It provides an ideal location for the PSO

4 It acts as a sump for psychiatric cases which otherwise would collect in holding units and medical units such as convalescent depots and general hospitals, which have no psychiatric facilities

The basic training programme can be divided into military training, physical training and recreation, Army education, medical and psychiatric supervision, general company administration, and welfare and padres. A special warning is necessary to prevent routine fatigues and medical inspection attendance from encroaching on the programme. The average routine stay in the depot should not be less than a month, but it is doubtful if any man benefits by a stay longer than 6 weeks

On arrival at the centre the men will be divided into the three main streams

1 Those who are truly convalescent—i e, the recently sick men.

2 The main training company

3 The hardening high-grade company into which likely material should be sifted at the earliest opportunity

On the basis of a 1000 bed unit, the ratio of company strength will work out as 1 : 3 : 1 Headquarters unit should cover all company fatigues and items of administration, and it is an advantage to have the high-grade company separated by some distance from the other two It should be easy to return patients from the rehabilitation centre to the filtration centre; as much as 10% may be returned This does not mean that their being sent to the rehabilitation centre has been premature, but it is a penalty of the dynamic policy, which is the most important feature of this organisation The psychiatric rehabilitation form initiated in the filtration centre should be passed on to the rehabilitation centre, and there should be free and frank interchange of views between the staffs of the two units, who operate as members of the same team

REALLOCATION

Final disposition should be rapid and as direct as possible to the unit, and all down-graded men should be seen by a PSO This interview should take place during the third week's stay at the centre, and the man should be held at the centre until it is possible that he can be posted direct to his unit or with a minimal delay to the intermediate holding unit. Transit camps are to be avoided as far as possible The medical officers at all holding units should be constantly reminded of their responsibility in handling psychiatric cases and instructed to handle them with benevolent firmness This should not preclude the occasional request for a reassessment but must definitely exclude the encouragement of neurotic sick parading The MOs and commanding officers of such units have a special responsibility in such matters and should inform their warrant officers and NCOs of the correct attitude towards ex psychiatric cases passed to them for disposal.

The above description implies that the staff is wholeheartedly interested in the problem in hand. It is utterly useless and indeed harmful to entrust this work to anybody who does not understand, or is not prepared to try to understand, the problems involved Finally I reiterate that the primary vehicle of our endeavours must be an atmosphere of dynamic activity

BASE PSYCHIATRIC UNIT: BASE PSYCHIATRIC WING OF BASE GENERAL HOSPITAL

Admissions to this unit should not constitute more than 10% of all cases, of which 5% represents cases for evacuation. The remaining 5% should be the cases of

genuine campaign neuroses and personality disorders These cases require very expert and intensive handling, and the unit should have the fullest clinical programmes. The atmosphere here may approximate to that of a well-run civilian unit, because the cases if properly selected are in men of high morale in whom the breakdown is entirely genuine

Discipline should be relaxed to the minimum necessary to administer the hospital unit Stay should be allowed up to 6 weeks but never longer than 3 months A valuable aspect of the unit's activities will be diversional therapy, one of the most valuable activities is husbandry In 1943 I placed 150 of my campaign neuroses on a farm in Tripoli The results were gratifying The term psychotherapy can be very misleading, but at this level it is capable of complete and sincere application

EVACUATION UNITS

There should ideally be wards of the main evacuation unit for the Command The clinical policy of such a unit will depend entirely on the facilities for evacuation. Where these are poor this unit will grow into a large unit, which will then raise the question of the provision of a base neuropathic general hospital, which will absorb the base psychiatric unit as detailed above. Such a situation arose in the ME in 1941 owing to the closure of the Mediterranean to Allied transport, but the discussion of such a unit is not the concern of this paper

Results

The above methods applied to the 8th Army made it possible to send 98% of men back to full duty, of whom not less than 30% returned to full battle duty The methods played a useful part in the total medical set-up, by conserving man-power, and it anticipated degrees of demoralisation which might not have declared themselves until the end of hostilities

Summary

The Army psychiatrist is concerned not only with the soldier's capacity to fight but also with his willingness to fight Although the general concept of psychoneurotic conflict is applicable to psychiatric casualties, the critical factor in two-thirds of the cases is morale The traditional view of the Army is thus essentially correct

Cases may be classified both according to their morale and according to whether the predominant symptoms are anxiety or dissociation These groups in turn can be divided into two subgroups. in the first the patient's behaviour is under his control, although he does have mild symptoms, in the second there is a degree of mental stress or anguish which produces torpor It is suggested that torpor is the true criterion of illness Men exhibiting it are usually of good morale

Methods and techniques are described, of which speed and vigour at the filtration level, a full therapeutic programme at the main filtration level, and good man management at the rehabilitation level are essential. The specific therapeutic techniques used have been ether abreaction and narcosis therapy

Problems arising from the soldier's acceptance of the rôle of invalid are discussed. Although the advantages of selection of recruits are emphasised, no reasons have been found to keep the potential neurotic from the combatant zone. Good morale will keep many a neurotic at work, and psychiatrists should be as much concerned with good leadership as with good treatment To meet these requirements an administrative set-up operating five procedures—filtration, treatment, rehabilitation, reallocation, and evacuation—is necessary These operate in general at three characteristic levels, and the work at each level is described With an organisation of this kind it was found possible in the 8th Army to return 98% of men to full duty, 30% being to combatant duty.

Prophylaxis is discussed, and the rôle of the junior NCO is mentioned as one of importance

The general psychiatric approach of this paper is pragmatic It accepts the fact that hereditary, constitutional, and familial factors are usually involved, and it sees that in most of the patients the organisation of the ego is so weak that their behaviour is influenced by unconscious motives to a greater degree than in more sthenic personalities Emphasis is placed on the promotion of morale through a special type of therapeutic discipline, which aims at creating effective ego ideals in relation to the defeat of the enemy, the creation of a sense of pride in the profession of arms, and a sense of loyalty to one's comrades and duty to one's country

Environment is important in handling the neurotic, and experience shows that a military environment can be provided which is as efficient as the usual hospital atmosphere. A direct military approach need not interfere with a sympathetic interest in the separate problems of each man, and is fully compatible with sympathy for suffering and respect for the inadequate man.

These methods, originally planned by Brigadier G W B. James, were put into operation under the administrative command of Major-General A. Galloway, with the general assistance of my immediate senior chiefs, Colonel L Rowlette, Colonel R M Savege, and Colonel J T McOuatt. It remains for me to refer to the work of Lieut -Colonel H B Craige, and finally to Corporals F Wright and A Graham, both of the RAMC, for loyal and valuable service.

URINARY EXCRETION OF COPROPORPHYRIN IN NON-ALCOHOLIC PELLAGRA *

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So long ago as 1909 Hausmann suggested that the sensitivity of pellagra patients to sunlight might be due to the accumulation of porphyrins in this disease. Since then numerous reports have appeared, some supporting the suggestion, others discounting it on the grounds that no large increase of porphyrin excretion could be detected

Interest in this matter was reawakened when Beckh, Ellinger, and Spies (1937), using a colorimetric method to determine porphyrin, said . "These studies show that increased porphyrinuria is an integral part of the pellagra syndrome and its presence can be used as an early objective test" They added that the coproporphyrins excreted might account for the photosensitisation observed in some pellagrins Nicotinic acid was said to restore the porphyrin excretion to normal not only in pellagra but also in various other conditions with porphyrinuria Unfortunately, the colorimetric method used was far from specific, and it was not long before their results and claims were subjected to severe criticism. Watson (1938, 1939) and Meiklejohn and Kark (1939) showing that urorosein is partly responsible for the colour reaction Watson and Layne (1943) have shown that the chromogen of the Beckh, Ellinger, and Spies reaction is also found in normal urines and bears no relation to deficiency of nicotinic acid.

Out of the resulting confusion contradictory claims have once again begun to appear. Watson (1938) has found, by a fluorimetric method of determination, increased porphyrin excretion in 3 out of 4 cases of alcoholic pellagra and improvement, although not to within normal limits, after nicotinic-acid medication. It was thought possible that the porphyrinuria in these cases might in part at least be due to hepatic insufficiency following the abuse of alcohol Layne and Watson (1943) said that 3 dogs on the Goldberger black-tongue diet maintained a normal excretion of urinary coproporphyrin uninfluenced by the onset of symptoms or medication with nicotinic acid. Dobriner et al (1938) reported increased porphyrin excretion in a alcoholic pellagrin; and similar but smaller increases in urinary and fæcal coproporphyrin have been observed in treated and untreated pellagrins by McAnally, Smith and Perlzweig (quoted by Harris and Harris 1941). On the other hand, Passmore et al (1940), investigating cases of stomatitis and glossitis in India attributable to defective intake of the vitamin-B, complex, found the urinary porphyrin without exception to be within normal limits Meiklejohn and Kark (1939) reported porphyrin excretion within normal limits in 4 cases of endemic

* The main conclusions reached in this study were stated by Z. Leitner during the discussion on biochemistry and psychiatry at the Royal Society of Medicine on May 24, 1945

pellagra, and Kark and Meiklejohn (1941) described 7 cases of pellagra (4 being alcoholic) in only 1 of which, an alcoholic, was there an abnormally high excretion of porphyrin

It is highly probable that the difference in experimental findings between different groups of investigators is in part to be explained by the degree of liver dysfunction in their patients Nutritional deficiences, such as pellagra, in poor people are often associated with chronic alcoholism, with a consequent likelihood of impaired liver function Nesbitt and Snell (1942), surveying various hepatic diseases, consider the degree of porphyrinuria to afford a fair index to the degree of damage suffered by the liver parenchyma A relation between liver injury and urinary excretion of porphyrin has also been suggested by other workers (Franke 1930, Riming ton 1939, Dobriner and Rhoads 1940, Localio et al. 1941)

In the present communication we bring forward evidence, obtained from 15 non-alcoholic pellagra cases in institutions, which strongly supports the conclusion that porphyrinuria is not an essential feature of pellagra *unaccompanied by alcoholism, and endorses the dictum* of Kark and Meiklejohn (1941) that an examination of the urine for increased porphyrin does not in any way aid in the diagnosis of pellagra We also record urinary excretion of porphyrin in 7 patients with Korsakow's syndrome, all these cases except one being attributable to alcoholism, but in only 2 was the output abnormal Finally, we include a case of beriberi in a publican who was a heavy drinker and whose porphyrin excretion was much increased

MATERIALS AND METHODS

The first ten cases in the accompanying table were in psychotic patients and have been described by Hardwick (1943), who has listed their symptoms and discussed their etiology

In nearly all the cases 24 hr specimens of urine were collected and the ether-soluble porphyrins determined in an aliquot by the fluorimetric method of Rimington (1943); in one or two instances random samples were all that could be obtained

As the upper limit of normal daily excretion of urinary porphyrin we have adopted the figure of 90 μg suggested by Kark and Meiklejohn (1941), although Dobriner et al (1937) place the upper limit at 120 μg, and Jope and O'Brien (1943) have found values up to 160 μg in a 24-hr normal collection Our experience supports the figure of 90 μg

DISCUSSION

Our experimental findings are recorded in the table That the 15 cases listed as pellagra were indeed examples of the condition is supported by the prompt and dramatic response in each patient to the administration of nicotinic acid (Hardwick 1943) They were also, except one or two cases, seen and confirmed as pellagra by Professor Sydenstricker All determinations of urinary porphyrin excretion were made before the institution of nicotinic acid therapy and only in cases 6 and 13 were values above 100 μg in 24 hr recorded * In case 6 a septic state, manifested by sores on the arms and hands may have contributed to the high figure, which was not altered by nicotinic-acid administration; and in case 13 some degree of liver dysfunction was apparent from the considerable quantity of urobilinogen present in the urine Case 11 deserves some comment

The patient a housewife aged 64, had had ten years *epigastric discomfort soon after meals* She was treated in outpatient departments and kept herself on a special diet which contained practically no meat She had a chronic cough for many years Nine months before our examination pulmonary tuberculosis had been diagnosed and she was sent to a sanatorium, where her condition improved for 8 months until she suddenly developed diarrhœa A few days later she had increasing anorexia accompanied by mouth ulcers which *almost made it impossible for her to eat*; then she suddenly became uncooperative and confused She was considered unsuitable for further sanatorium treatment and was sent back to hospital

On examination she was irritable resentful, confused dis orientated and wasted body weight 5 st 12 lb., face red and

URINARY COPROPORPHYRIN EXCRETION IN NON ALCOHOLIC PELLAGRA, KORSAKOW'S SYNDROME DUE TO ALCOHOLISM AND BERIBERI

Case	Diagnosis	Age	Sex	Urine void in 24 hr (ml)	Porphyrin excreted in 24 hr (µg)
	Pellagra plus				
1	Imbecility	30	F		18
2	Catatonic schizophrenia	41	F	1260	7 6
3	Chronic "	38	F	1100	6 4
4	Paraphrenic "	60	F		98
5	Schizophrenia	40	F		59
6	*Ditto with septic sores* (After 35 days' treatment with nicotinic acid)	42	F	1170	103
7	Schizophrenia	40	F		118
8	Ditto (5 days later)	35	F	1050	67
				1810	105 5
9	Schizophrenia	55	F	1193	47 7
10	Delusional insanity	60	F	1136	36 8
11	Pulmonary and intestinal tuberculosis	64	F	880	11 9
	Ditto (39 days later)			1600	54
12	*Schizophrenia*	47	F	1350	2 5
13	Ditto (excess of urobilinogen)	40	F	2016	154 8
14	Schizophrenia	43	F	716	33 2
15		46	F	1515	31 7
16	Korsakow's syndrome	32	F	1100	11
17		48	F	1620	41
18		48	M		135
	Ditto (3 months later)			1380	60 2
19	Korsakow's syndrome	6[illegible]	M		81
	Ditto (3 months later)			1100	51 7
20	Korsakow's syndrome	59	M		58
	Ditto (3 months later)			1370	47 4
21	Korsakow's syndrome	49	M	930	140
22	Ditto with diabetes insipidus (has never been a drinker)	54	M		20
23	Beriberi in a heavy drinker	41	M	600	360
	Ditto (45 days later after lb and marmite medication followed by pronounced improvement)			130	318

scaly, resembling sunburn, especially at the nasolabial folds and round the eyes The back of both hands and fingers, as far as exposed to the sunlight, were red scaly and infiltrated with deep bleeding fissures over the right metacarpo phalangeal joints Dry fissure of upper lip angular stomatitis with cracks; tongue deep red smooth denuded, and shiny with atrophied papillæ partly fissured scattered small ulcers visible. Sputum tubercle bacilli present ESR 37 mm per hour Hb 62% Red cells 4 900 000 Colour index 0-6 Mean red-cell diameter 6 6μ White cells 12,000; differential count normal Complete achlorhydria Urinary porphyrin on two occasions 11 0 and 54 μg in 24 hr Slit lamp examination (Professor Sydenstricker) showed extensive corneal vascularisation. On combined nicotinic-acid and riboflavine treatment her mental condition and her face improved within a week, her hands and lips in less than three weeks The patient died six months later, and the PM revealed extensive intestinal tuberculosis besides the pulmonary lesion

This case-history illustrates how, for instance, a sudden onset of diarrhœa due to intestinal tuberculosis may precipitate the development of a pellagrous condition. The sequel of events appeared to be diarrhœa, anorexia, sore mouth, inability to take food, depression, and confusion, leading up to typical fully developed pellagra

The case of beriberi (No. 23) is also informative

Patient has always been a heavy drinker mainly whisky gin and beer and recently he has taken *hardly any food*. He has previously been healthy and has had no major illness Shortness of breath first arose a year ago About two months ago he felt weakness of his legs followed by pains and cedema, and for two weeks was completely bedridden On examination he showed complete absence of tendon reflexes, tenderness of the limbs, gross œdema anasarca and ascites dilated heart, and congested lung bases Liver enlarged below umbilicus. Electrocardiogram of very low voltage *Porphyrin excretion* on admission 360 μg in 560 ccm of urine output in 24 hr He had daily injections of 25 mg of aneurine and ½ oz. of Marmite orally and his symptoms including heart failure peripheral neuritis and œdema, disappeared Six weeks later there was only a small amount of ascitic fluid left whereas the porphyrin excretion in 24 hr was still 318 μg

* In case 5 the mean of two pre-treatment values was 89·25 μg

CONCLUSIONS

It appears from our results that, although pellagra uncomplicated by alcoholism is not accompanied by increased porphyrin output in the urine, neither is alcoholism per se necessarily sufficient to excite this symptom, if one may judge from the 6 cases of Korsakow's syndrome in alcoholics only 2 of whom showed abnormally high porphyrin excretion. A combination of circumstances or deficiencies contributory to particular types of hepatic lesion may be requisite before porphyrin elimination becomes disturbed. The relative frequency with which an increased amount of urinary coproporphyrin has been reliably reported in cases of pellagra plus alcoholism is of considerable interest in this connexion, and one is tempted to speculate whether the combination of factors, deficiency due to restricted or unbalanced diet plus toxic assault, may play the same part here as has been shown, for example, in the case of arsphenamine poisoning reported by Messinger and Hawkins (1940), or the case of chronic hepatitis of alcoholic ætiology complicated by the sprue syndrome reported by Leitner (1942), or the now numerous examples of the protection afforded to the liver by methionine against injury by such toxic agents as chloroform, &c.

The case of beriberi is interesting in that, in spite of dramatic improvement in the clinical condition brought about by appropriate therapy, the porphyrin excretion remained unchanged, indicating presumably a permanent hepatic lesion.

SUMMARY

Urinary coproporphyrin excretion has been found, except in two cases explicable on other grounds, to lie within normal limits in a series of 15 non-alcoholic pellagra patients whose prompt and satisfactory response to nicotinic-acid medication substantiated the diagnosis of their condition.

In a series of 7 patients with Korsakow's syndrome, in 6 instances referable to alcoholism, only 2 showed abnormally high urinary porphyrin excretion.

A case of beriberi (alcoholic) had a marked porphyrinuria, which remained unchanged despite appropriate medication and much improvement in general condition.

These studies further emphasise that porphyrinuria is not an essential feature of pellagra, and that determination of urinary porphyrin does not in any way aid in the diagnosis of the condition. Alcoholism per se appears to be insufficient necessarily to produce porphyrinuria.

The factors or combination of factors which may lead to porphyrinuria in persons with pellagra, simultaneously exposing their livers to assault by quantities of alcohol, have been considered in the light of recent findings relating extent of hepatic injury to level of intake of an essential factor, such as protein or methionine, in the presence of a toxic agent.

We are grateful to Sir Allen Daley and Dr R. C. Harkness for the facilities which were placed at our disposal to carry out these investigations in various LCC hospitals, and to the several medical superintendents and medical officers concerned, particularly Drs. W A Caldwell, E Davis, B Gottlieb, and S W Hardwick, and Prof S Nevin We are also greatly indebted to Sir Philip Manson-Bahr and Prof. V P. Sydenstricker for generous help and advice.

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MUSTARD-GAS BURNS

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ON April 24, 1944, a boy, aged 17, stole a 6-lb. canister of mustard-gas from an ammunition store He opened the canister the same evening and poured the fluid into two mineral-water bottles. While doing so he splashed some of it on his hands and wiped most of it off with grass He then placed the two bottles out of sight in a corner of the garden of his home.

Next morning his hands were sore and blistered, and there were blisters on his right knee and right great toe, but he did not associate them with the fluid he had been playing with the previous evening During the day the blisters coalesced and were seen by his doctor, who prescribed sulphanilamide powder and calamine lotion He, along with 18 other persons, was subsequently admitted to hospital and treated for burns. His case was not one of the more serious ones and therefore does not require special description.

CASE-RECORDS

CASE 1 —*Fatal burns* On the evening of April 30 at about 6 PM the boy's sister, aged 7, found one of the bottles containing about 1¼ pints of liquid mustard-gas and loosened the stopper She shook the bottle vigorously, spilling about ½ pint, some of which splashed over her She ran into the house, crying and complaining that her eyes were burning Her father noted that she had some of the yellowish brown liquid on her hair and on the front of her dress, but he did not see any on her face Her eyes were closed, and she complained that they were burning Within 2–3 min of the accident he bathed them with tap-water and later with boracic lotion. Half an hour after the contamination her mother washed her hair with soap and water, rinsing it well, and removed her clothes

At 8 30 that evening the child was taken to the casualty department of the hospital, but the true nature of the condition was not then recognised, there being only a very slight erythema of the medial aspect of the right thigh Her eyes appeared normal, and she was considered fit to go home, but that night she was restless and vomited 5 times Next morning, blisters were seen on her right thigh and she was admitted to hospital at noon, 18 hr after the accident. She was then in a severely shocked condition. Her pulse rate was 190, pulse of very poor volume, and temperature 95° F. Her respirations were shallow, 34 per min , and blood-pressure 100/70 She was restless and in semi-coma but was not aphonic. During the first 3 hr after admission she vomited once, there was well-marked œdema and pallor of the face, especially of the eyelids, and slight exudation at the lid margins, but no erythema. It was not possible to open the eyelids without causing great pain, but there was no lesion of the eyeballs On the right cheek there was a blister ¾ in. in diameter, and round the lips were numerous small blebs There were also 3 small blisters under the chin On the dorsal aspects of both arms and hands were erythema and many blisters of various sizes, but the palms of the hands were unaffected The blisters were of the solid type, containing fibrin clots

Three-quarters of an hour after admission nikethamide 2 c.cm was given by intramuscular injection with slight improvement An hour after admission a blood examination showed red cells 5,510,000 per c.mm , hæmoglobin 102% colour-index 0 9. For this reason no transfusion was given.

Three hours after admission she was given morphine gr ¼ and atropine gr 1/150, and ½ hr later, under very light gas-and-oxygen anæsthesia, the affected areas were cleaned with 'Cetavlon,' the blistered skin removed, and 2% sulphanilamide cream applied

The patient withstood the operation well Her general condition when she left the operating-theatre showed no appreciable deterioration. At 6 30 PM on the same afternoon she was examined by Prof J A. Nixon, and at this time no signs of tracheitis, bronchitis, or bronchopneumonia were noted, although the facial œdema was increased and now pitted on pressure

At 2 AM on the next day she had a dry cough and was rather restless Aphonia seemed to be present at this time As she had not passed urine since admission, a catheter was

passed and 8 oz was withdrawn. It contained albumin At 3.30 AM morphine gr ¼ was given, and she became less restless At 6 AM the cough was still troublesome, but at 8 AM it was more loose and productive She then seemed slightly "bubbly," and there was some cyanosis. Signs of tracheitis, bronchitis, and early pulmonary œdema were now present Her temperature rose to 101° F and her pulse rate to 200 the pulse being now of very poor volume Continuous oxygen was administered and nikethamide 2 c cm given

At 10 AM she passed into complete coma, and at 12.40 PM, 42½ hr after contamination, she died.

Summary of autopsy report—There was necrosis of the mucous membrane of the pharynx, larynx, and trachea The affected surfaces were grey and sloughing and a membranous coat similar in appearance to that of diphtheria had formed Pus could be squeezed from the bronchi, and bronchopneumonia was found microscopically There was interstitial emphysema especially in the anterior parts of the lungs. The tissues of the neck were œdematous, and the cervical lymph-glands were enlarged and soft Most of the mucosa of the stomach had sloughed and bloodstained fluid was present in the lumen.

The burns of the skin were mainly superficial but some were deep Sections of the burns of the thigh showed that where blisters had developed the separation was between the epidermis and the dermis Except for their mouths the hair follicles were intact In the deeper burns the epidermis was missing and the superficial part of the dermis necrotic, but the deeper parts of the hair follicles had survived

The eyes did not show any damage either grossly or microscopically No changes were found in the liver heart, or brain Some of the convoluted tubules of the kidneys showed necrosis and a deposit of granular basophil material The cervical lymph-glands showed acute inflammation and depletion of lymphoid tissue

On May 1, the day on which the above case was admitted, seven other cases were brought to hospital, four being brothers and sisters of the above child, including the youth who first obtained the mustard-gas On the 2nd six cases, on the 3rd four cases, and on the 5th one last case was admitted Some of the patients were children who had played in the contaminated garden, others were affected by contact with those children or their clothes One adult and one child were affected merely by walking in the lane outside the garden. The adult had a burn on the face, and the child one on the knee In three others, one of whom had typical severe burns on the abdomen and thighs, no contact could be traced

CASE 2—*Severe respiratory involvement with recovery* A boy, aged 9, who gave no history of contact with the mustard gas but lived near the house of the previous patient, felt sick and vomited on April 29 Next morning the back of his right hand was painful and red, and later in the day it blistered On the morning of May 1 the skin of his abdomen and right side of his face was red and painful and there were a few small blisters on his abdomen He complained of slight loss of appetite and of a burning sensation in the affected areas

He was admitted to hospital on May 2 at 1 30 PM, about 53 hr after the onset of the first signs. His general condition was fair and he had no pain His temperature was 98° F, pulse rate 86, respiration 22 and blood pressure 105/75

There was erythema of his whole face, especially on the right side, and a bilateral mild conjunctivitis His whole anterior chest wall was erythematous, varying from bright red to dusky violet and there were numerous small blisters The right axilla and upper arm were also erythematous and showed a few small blisters The skin of the whole abdominal wall was bluish red with many small blisters giving a crocodile skin appearance A few large blisters were present the largest being in the left iliac fossa and measuring 1½ in in diameter This was of the solid type and later proved to be a deep burn There were small blisters of the dorsum of the penis with diffuse erythema of the scrotum penis and perineum and well marked œdema of the prepuce There was a deep burn of the dorsum of the right hand and webs of the fingers, and there were large blisters over the knuckles On the medial aspect of the left knee there was a small area of erythema, and a similar area on the right knee with some vesiculation The burns were mainly superficial but some areas were deep In all about 30% of the body surface was affected

At 3 30 PM on the day of admission under light gas-and oxygen anæsthesia the affected areas were cleaned with cetavlon The blistered skin was removed and 2% sulphanilamide cream applied Next day the child was restless Blood examination showed: red cells 4 750 000 hæmoglobin 92% colour index 1·0; white cells 12,200 neutrophil polymorphs 70% There was no albuminuria

On May 4 the patient seemed slightly cyanotic erythema of the whole of the back was noted with a blister 1 in in diameter on the right buttock Smaller ones later developed between the scapulæ Similar treatment was applied to these His pulse-rate rose to 122 and his temperature to 100° F His respirations were 26 per min A few râles were present in his chest and he developed a loose cough Sulphamezathine tablets were given, 2 g statim and 1 g four hourly for 72 hr Next day the cough was still present Oxygen was given Radiography of the chest showed nothing abnormal On the 6th his general condition was much improved but he still had a slight cough. On the 8th the improvement was maintained Blood-count showed: red cells 4 240 000 hæmoglobin 74% white cells 13 000, neutrophil polymorphs 64%.

On May 10 the patient was much better and the dressings were removed for the first time on this the 8th day Some of the more superficially burnt areas were healed and showed a copper or brownish pigmentation All other areas were clean, except one near the penis and perineum A swab taken from this region showed coagulase positive *Staphylococcus aureus*

Next day the patient was comfortable, but the penis remained œdematous, and slight exudation was present a swab from which yielded coliform organisms *Staph albus* and *Micrococcus tetragenus* On May 12 the hand sloughs were separating On the 13th *Staph aureus* was cultured from the exudate By May 16, the 14th day after admission to hospital, all areas were healed except small scabs on the dorsum of the right hand and in the right iliac fossa and a moist area 1 cm in diameter on the dorsum of the penis These healed within the next week. There was slight stiffness of the fingers of the right hand at first but this rapidly improved with exercise, and the patient was completely well by June 1

The brownish pigmentation remained and was very noticeable in the right axilla and both groins A gradual desquamation of the skin subsequently took place The patient was discharged in the 7th week.

In the other 17 cases the lesions were confined to the skin In all of them there was a latent period of 8–24 hr before the signs developed Erythema first developed, then blistering The blisters, especially when large, were of the solid type

TREATMENT

The cases in this series were first seen at stages varying from 18 hr to a few days after contact with mustard gas; hence preventive treatment could not be carried out. It was decided therefore to treat them as ordinary thermal burns In the children light gas and-oxygen anæsthesia was employed for the initial cleansing of the skin, but in most of the adults no anæsthetic was used The cleansing was done as early and as thoroughly as possible with swabs soaked in 1% cetavlon The blisters were opened with swabs, and the loose epithelium peeled off or removed with scissors Cream containing either 2% or 10% sulphanilamide was then applied to the raw surfaces, the weaker cream being used where the burns were extensive: 'Lanette wax SX' 10 g, ol ricini 25 g sulphanilamide 2% or 10%, glycerin 10 g., and water 45 g Gauze or tulle-gras was used for dressing The dressings were left on for 7–10 days to avoid cross infection When the first dressing was removed, most of the superficial burns were healed but the deeper ones usually required fresh dressings of sulphanilamide cream and this was continued at intervals of 5–6 days until healing took place

COMMENT

In this series of cases the results of local treatment conformed with those which we have had with ordinary thermal burns The superficial burns were healed in 10 days and the other deeper burns, none of which were very large in 7–8 weeks

Aspiration of the blisters is advised by some authorities, but if blisters are numerous or solid this is obviously impracticable, and it is then better to open them and remove the epithelium so that the antiseptic treatment may be applied to the new surface

The coppery pigmentation which usually follows the burns was well seen in nearly all the cases, but this gradually disappeared with the desquamation of the superficial layers of the skin.

The patient who developed chest signs but recovered appeared to benefit from sulphamezathine. Since mustard-gas is toxic to the bone-marrow, objection may be raised to the too ready giving of sulphonamides, but the leucocyte-count in this case did not show any signs of toxic action.

A point of some importance is that in the first case, where liquid mustard-gas was apparently splashed on the face, there was considerable œdema with only little vesication, and the eyes were not affected This may well have been due to the eyes being washed with water immediately after exposure, supporting strongly the advice generally given to do this as first aid.

SUMMARY

A boy stole a canister of mustard-gas and opened it. He and 18 other persons became contaminated with the poison One died from burns of the respiratory tract; immediate washing of the eyes may have prevented ocular damage in this patient

Most of the skin burns healed well after cleaning with cetavlon and applications of sulphanilamide cream

We wish to thank the members of the honorary surgical staff of the Cardiff Royal Infirmary for permission to publish these cases

Reviews of Books

Pulmonary Tuberculosis in the Adult

MAX PINNER, MD, chief of the division of pulmonary diseases, Montefiore Hospital, New York, editor, American Review of Tuberculosis, clinical professor of medicine, College of Physicians and Surgeons, Columbia University, New York (Charles C Thomas Pp 579 $7 50)

THE most exciting books are those which not only add to one's fragmentary knowledge of a subject, but also give the fragments a twist so that they fall into a pattern which makes sense where before was chaos. Our knowledge of pulmonary tuberculosis is fragmentary, the basic indisputable facts are few, their distortion by preconceived prejudices is procrustean Dr Max Pinner has set out to piece together basic facts and seasoned hypotheses into a pattern which is plausible and, in his own words, "consistent within itself" And he has succeeded Where there are missing links in the pattern, he boldly draws attention to them Where there are alternative solutions he displays them all, weighs them up and puts forward his own personal choice In his preface he makes the modest disclaimer—" . This book does not attempt to tell the student how to diagnose the disease nor how to treat it; [nor] . how to do this that or the other thing in the practical performance of the clinician's (or the pathologist's or the bacteriologist's) duties" This is true only in the narrowest sense, for nobody could possibly study this work without gaining a clearer conception of the disease he was combating, and a deepened understanding of the whys and wherefores must necessarily lead to a more intelligent appreciation and better application of technical procedures.

Though there is a steadily developing chain of reasoning throughout the work, it falls roughly into three sections The first four chapters give a character-study of the tubercle bacillus, describe in detail the different tissue-reactions to infection and their pathogenic determinants, and lead to a logical digression on the problems of immunity and the rightful place of tuberculin The next section deals with the initiation of active disease in all its different manifestations (from primary complex to bronchial tuberculosis) and its clinical revelation by the exercise of diagnostic principles and laboratory procedures Before embarking on discussion of surgical interference, Dr Pinner has assembled a unique symposium on the physiological principles of respiration, where all terms subsequently to be used are clearly defined, and this chapter leads naturally to a clear exposition of the principles of collapse therapy. Medical treatment comes late in the book and thus appears to receive less emphasis than the ancillary measures. Stress is laid upon strict bed-rest—strict physical rest—but no indication is given of the importance of mental or emotional rest. This is really the only notable omission in the book and is all the more remarkable in these days of psychosomatic enlightenment, when it is generally realised how despotically the psychological "inner" milieu can govern progress and prognosis Constitutional, environmental, socio-economic factors, et al, in the war between tuberculosis and the community, however, are carefully assessed in the final chapter on epidemiological principles

At the end of each chapter there are the usual references to the relevant literature, but also after each reference is a comment, sometimes a sentence, sometimes a précis and appraisal of the work in question, all of which serve their purpose as guide-posts to more complete information. These miniature abstracts supply nearly a quarter of the bulk of the reading matter

The Tissues of the Body

An Introduction to the Study of Anatomy (2nd ed) W E LE GROS CLARK, FRCS, FRS (Oxford University Press Pp 388 21*s*)

THIS second edition is but a few pages longer than its predecessor, yet a considerable amount of new information, derived from recent research, has been skilfully woven into the text Revision and rearrangement have been managed without altering the general layout of the text; a few illustrations have been replaced by new ones, and there are some welcome additions. This stimulating account of body mechanisms, illuminated by sidelights from pathology, endocrinology, tissue culture work, and other sources, may profitably be read by students of all generations.

Opposing Aspects of Social and Political Thought

F PARKES WEBER, MD CAMB, FRCP, W. HENRY LEWIN (H K. Lewis Pp 34 2*s* 6*d*.)

Mr Lewin has produced in booklet form a correspondence between Dr. Parkes Weber and himself in which their views on some problems of biology, ethics, and politics are exchanged The lines of thought on which the opinions of the writers are evolved remind one forcibly of William James's antithesis between the "tender minded" rationalist and the "tough-minded" empiricist The data provided by biological and sociological observation equip Mr Lewin with positive views which point to clear-cut courses of action, on individualistic lines Dr Parkes Weber, while seldom disputing the major premise, is restrained by his "gospel of doubt" and for the most part emerges as the advocate of middle courses. As a disputation between two mature and penetrating thinkers the correspondence will provide stimulus and pleasure to many.

Clinical Aspects of Sepsis in Gunshot Wounds

Prof A. V MELNIKOV, colonel of Red Army Medical Services, translator, Dr S Yale (Medical Publications Pp 176 15*s*)

FIERCE fighting, difficulties of transport, and appalling weather conditions made sepsis in gunshot wounds a far more serious problem in the armies of our allies on the Eastern front than it was in any of the campaigns in which the British armies were engaged. Professor Colonel Melnikov records his views and his experiences, basing his conclusions on 100 cases treated in the Kirov hospitals and a large number observed during his work as a surgeon with the Red Army Medical Service He uses the word "sepsis" to indicate a grave systemic infection, rather than in the more general sense of invasion of tissues by pyogenic micro-organisms The treatment of this serious group of cases has been by radical surgery, transfusion, and, in the case of limb injuries, immobilisation in plaster-of-paris Sulphonamide therapy is dismissed briefly, and penicillin was not available at the time when these observations were made Of the 100 cases observed at Kirov 35 died.

The difference in experience and outlook, the extreme degree to which classification is carried, and the use of familiar terms in an unfamiliar sense make this book difficult reading, but it is essential that all should study it who wish to gain an insight into the difficulties under which the medical services of our Russian allies have been working, and the courageous way in which these difficulties have been tackled.

THE LANCET

LONDON SATURDAY, OCTOBER 20, 1945

Doctors for Industry

A COMMITTEE set up by the Association of Industrial Medical Officers[1] holds that "no national health service can be adequate that does not include, as an integral and properly coördinated part of the whole, an industrial health service," and regrets that "so far, no plan of any kind for the development of this service has been evolved by a responsible Government department" But believing that national provision of an industrial health service cannot and should not be long deferred, it maintains that "adequate facilities for education and training of those doctors, nurses, and others who take part in it must be provided at the earliest opportunity This is an opinion which is easy to share Never at any time was there more opportunity or more reason for encouraging the development of the industrial health services War time experience in factories has proved not only their social but also their industrial value it is generally recognised that they have aided efficiency, increased production, and reduced absence of workers through minor illnesses and injuries

Hitherto the full development of such a service has been handicapped by lack of people trained, or available for training, in this specialised work As demobilisation proceeds, many doctors, nurses, and orderlies seeking fresh employment may be attracted to this new and important branch of medical practice, and it should not be difficult to recruit enough men and women to satisfy the full needs of the service, if only they can be offered proper training and pleasant enough prospects thereafter The committee leaves us in no doubt about the scope and variety of the work to be done in connexion with factories, mines, quarries, docks, shipbuilding yards, railways, shipping, the building industry, agriculture and commerce—not to mention research and teaching But when it turns to the provisions so far made for training in industrial medicine it finds them very far short of what is needed Recent developments, including the foundation of chairs or readerships in industrial health at Manchester, Durham, and Glasgow, are helpful, but it would like to see similar departments in the universities of London, Birmingham, and Liverpool Moreover, throughout the teaching of medical undergraduates, more should be said not only about the effect of occupation on illness but also about the economic repercussions of illness on the patient and his family The student should learn to recognise that when he treats a patient, the 'treatment is not complete until he is again able to earn his living" The committee demands that "teachers of medicine and surgery should themselves understand something of the principles of industrial health" It suggests, too, that the student should have 'a course of at least six lectures on occupational medicine and spend at least three days within the factory when the normal work of the industrial medical officer can be explained to him"

The main vocational training of those who seek a career in industrial medicine, will, however, not begin until after qualification indeed, the committee does not want it to begin until the aspirant has had, after qualifying, "at least two years in which to gain clinical experience, both in house appointments and in general practice" It will then be necessary "to offer three distinct types of training (i) for the man who is to devote his life to this type of work and who intends to become a consultant in it, (ii) for the man who intends to become an industrial medical officer, whether part time or whole time, and (iii) for special appointments (such as those of the present examining surgeons and factory medical inspectors)" (The apparent implication in this grouping is that medical inspectors of factories are not to be classed as consultants, but the truth is that no other group of doctors has had a wider experience of industrial affairs and none has a better claim to consultant rank.) From this the report goes on to differentiate between the type and length of training needed for these different groups For our part we could have wished that the committee had concentrated more on the steps necessary to attract and train a much larger number of part time and whole time industrial doctors, for these are the men and women needed now Doubtless in their ranks suitable candidates will later be found to train as consultants, teachers, research workers, and medical inspectors of factories, and admittedly, all these groups will have to have a longer and more specialised training than the ordinary works doctor But would it not be better for them to have this special training after they have gained practical experience in industry, rather than make an academic decision to specialise while still at hospital or university?

However this is decided, the urgency lies in the training of the rank and file, and we are glad that the committee everywhere recognises the necessity of training for part-time as well as whole time service The part-time industrial doctor (usually spending the rest of his time in general practice) can play an important part, for much of the industry of this country is organised in units which are too small or too scattered profitably to use or to share the services of a whole time medical officer In the proposed syllabus of training prominence is rightly given to the physiology and psychology of work, the principles of social and preventive medicine and the working environment, and to reablement and resettlement in industry Naturally, occupational diseases have also to be studied, but they are not allowed to dominate the picture If we are designing a service that will bring health to industry, rather than one that will merely treat industrial disease, this is the right approach

Finally, the committee discusses the advisability of offering diplomas in industrial health Despite strong arguments which it draws from the experience of other specialties it eventually decides that such a diploma is now a necessity and 'recommends that if a Diploma in Industrial Health is instituted it should be given by the Royal Colleges It would not be in the best interests of industrial medicine if

[1] The members were Dr W E. Coleman (chairman), Dr J C Bridge Dr Donald Hunter Dr R F Lane, Dr J A Lloyd Davies Dr T Gwynne Maitland Dr D C Norris Dr C L Pots Dr R. S Schilling Dr Donald Stewart and Dr K M A Perry (secretary)

diplomas in the subject were instituted by separate universities or other bodies throughout the country." This last eventuality, however, seems not unlikely As announced in our issue of Oct 6, the Society of Apothecaries of London have already declared their intention of granting a special diploma, and other examining bodies may follow In our view it is important to train as many doctors for industry as is feasible, but the course of training of three (or at most six) months sufficing for this purpose would hardly justify the award of a special diploma If the establishment of a diploma were to have the effect of excluding from industrial posts all those who did not possess it, a disservice would undoubtedly have been done to industry For those who do seek academic recognition of special study and special experience in this branch of medicine, an alternative would be to modify the course for the diploma in public health so that (after initial training in environmental and preventive medicine) the candidate could specialise in different groups of subjects, one of which might be industrial medicine The new syllabus proposed in a report from the Society of Officers of Health (see p 514) includes a basic course for doctors undertaking any form of public-health work

Normal Life of the Red Cell

BECAUSE it is easily removed from its normal environment and easily replaced, more is known about the behaviour and chemistry of the blood than of any other tissue But there is still much speculation about the individual red cell Is each cell just a protoplasmic mass, an envelope for the carriage of hæmoglobin, or is it a tissue cell which by evolution has lost its nucleus but retains the biological property of having a more or less fixed life? On the former view one would expect that destruction would be indiscriminate, on the latter that each cell would live its normal life-span, wear out, and be removed at a set time, which could be determined

Many attempts have been made to estimate the average life-span of the individual red cell through transfusion experiments ASHBY[1] in 1919 evolved a technique for identifying heterologous but compatible transfused cells in a recipient's circulation—e g, O blood in an A recipient The principle of this method is to count the donor's cells by using as a diluting fluid not Hayem's or another routine diluent but a serum which will completely agglutinate the recipient's own red cells, leaving the donor's cells unagglutinated By following the inagglutinable cell-count from the time of transfusion until it reaches the low level of the pretransfusion "blank" count, one can calculate the life of the donor's red cells in the recipient's circulation ASHBY's own early results were somewhat variable, but later modifications of the method have increased its accuracy Using DACIE and MOLLISON's[2] modification, CALLENDER and her colleagues[3] in WITTS's department at Oxford have confirmed the estimate of ASHBY and others[4,5] that the life of the red cell under these conditions is about 120 days Unlike most of the previous workers they used normal subjects as the recipients These subjects had been bled over the preceding few hours an amount of blood equal in red-cell content to that of the blood transfused, so that the recipient's erythropoiesis was disturbed as little as possible Their careful follow-up of the elimination of the donor cells showed that, apart from a slightly increased rate of destruction in some cases in the first few days, a fixed proportion of the blood was eliminated each day. From this it was possible to prove mathematically that each cell must live for a fixed time and then be destroyed. It would have been preferable in these experiments to have used absolutely fresh blood instead of blood stored up to six days, otherwise the planning of the experiment was admirable In almost all the previous investigations the subjects were suffering from some form of anæmia or other disease, or were normal persons under conditions of considerable physiological stress When normal subjects have been used the methods of examination have often been open to grave criticisms Oxford workers[5] had previously shown by the Ashby method that in certain diseases and anæmias the destruction of transfused cells, while directly proportional to time, was more rapid than in the normal subject On the other hand, in some hæmolytic anæmias the elimination curve was not linear but roughly exponential The factors which produced curvature in the decay curve resided in the recipient and were probably related to his disease Indiscriminate destruction of red cells, regardless of their age, would give an exponential decay curve This indiscriminate process may be active in some hæmolytic states

It is sometimes possible to deduce the life-span of the red cell mathematically—for instance, from the time the red-cell count takes to reach its maximum when man is exposed to low atmospheric pressure at high altitudes[6] or from the time it takes to return to its pretransfusion level after transfusion of large amounts of blood (as in cases of aplastic anæmia), or from the time it takes to reach the normal level again after a hæmorrhage[8] These deductions give a life-span of 14–35 days But it is notable that the subjects of the experiment have grave disturbances of erythropoiesis either from disease or from physiological stress SCHIODT,[8] who summarises much of this work, also quotes the observations made on pigment excretion, from which it is possible to calculate the red-cell life The average amounts of bilirubin excreted daily by patients with bile fistulæ can be assessed, and from these figures red-cell life has been estimated as from 15 days[9] to 40 days,[10] but part of the bilirubin produced by red-cell destruction may be retained[11] Urobilinogen excretion has also been used as a basis for the calculation If no urobilinogen were re-absorbed and used again, the life-span would be 100–200 days, but it is claimed that three-quarters of the total produced is re-absorbed[12] WATSON[13] severely criticises almost all the methods used for measuring the daily excretion of urobilinogen

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doubts the validity of the assumption that hæmoglobin changes quantitatively into bilirubin, but taking 300 mg as the most reliable estimate of the bilirubin in the 24 hourly bile[11] concludes that the daily wastage of hæmoglobin is 0 8% and the life of the red cell 140–160 days Thus from the same published figures the answer can be deduced as under 50 or 150 days

Results equally difficult to interpret are obtained by another method It is possible to calculate the life-span of the red cell from that of the reticulocyte, if one knows the percentage of reticulocytes in the circulating red cells BAAR and LLOYD[12] hold that the reticulocyte's maturation time of 24 hours or more as previously determined is too long Their own results show a linear decrease in the reticulocyte counts during the first 4 hours or so of incubation and then a progressive slowing of maturation They attribute this retardation to necrobiotic changes in the cells, and calculate the maturation time as 7 hours by extending the linear part of the decay curve The postulate of necrobiosis is, however, untenable *It was made because the cells showed an altered* osmotic behaviour with hypotonic saline, a phenomenon which MAIZELS and PATERSON[13] have shown does not affect the viability of the cell On the basis of a 7-hour reticulocyte maturation time BAAR and LLOYD deduce a 42 day life for the whole red cell, a figure which on the evidence is too low They have attempted to confirm the 42 day life by another method They transfused normal blood to patients with acholuric jaundice and tried to follow the survival of the transfused blood by analysing the recipients Price-Jones curves into donor cells and recipient's cells—a method bristling with assumptions, one being that the donor's cells maintain a pre transfusion morphology in the recipient's plasma until their elimination Even if this and other assumptions were tenable the recipients had gross abnormalities of erythropoiesis and erythroclasis, so deduction of the normal life-span of the red cell from these data is impossible

Up to now, though the Ashby method they use has not entirely escaped criticism, the results of the Oxford workers seem to give the nearest approach to a reliable answer to this problem

Future of the Ministry of Food

IN the war of 1914–18 a special Ministry was established to regulate the supply and consumption of food and encourage its production" This Ministry came to an end in 1921, by which time it had no longer any useful function Its chief service to the nation was its discovery of means of enlarging the bottlenecks through which food passes on its way from producer to consumer, and of controlling the price the consumer pays So essential are these powers to a war time economy that the Ministry was hastily resuscitated in 1939, and it has since fulfilled its functions in a way which has on the whole won general approval The food resources of the country have been more equally distributed than ever before

On each occasion the Ministry has been set up to deal with a grave emergency, and the question arises whether we are now to prolong its life indefinitely into an era which we hope may be peaceful Should it become a permanency, or relegate its functions to other departments such as the Ministries of Health and Agriculture? Le Gros CLARK,[18] who tabulates the "weighty arguments" in favour of permanency, also points out that they must be accepted with reserve Much of the success of war-time nutrition we owe, he says, to high employment and good wages rather than to the direct action of the Ministry of Food, and unless the Government pursues a policy of high employment and high wages in the years to come we cannot expect a permanent Ministry of Food to be of much value Also, when food is no longer scarce, will it be reasonable to preserve a Ministry which was called into being to mitigate the effects of shortage? Unfortunately for this last objection, and for the public, there is no immediate prospect of abundance of food in Great Britain and a world shortage for many years to come is inevitable It is for these reasons that, though the Ministry of Food would doubtless benefit by reconstruction, its immediate liquidation would be a grave mistake If it disappeared, the production and distribution of food would presumably fall into the hands of a number of marketing boards in which, judging by precedent, the producers and distributors would be represented, but not the consumers One function of a reconstructed Ministry should be to represent the consumer on these boards Another function, at least equally important, should be to coöperate with the main food-producing countries, whether of totalitarian or individualist economies, in regulating the flow of food into our markets It is difficult, indeed, to see how the ideals of the Hot Springs conference can be realised in this country without a Ministry of Food, for the future production and consumption of food cannot be left to the "laws" of old fashioned economics

To keep agriculture on its present footing—and a sound agriculture is a prime necessity for any country in the world—the Government will have to guarantee to farmers a fair price for their products And if guaranteed prices and subsidies are to be the rule the Government may, as in war time, have to take action against inefficiency in farming If the production of food is considered to this extent to be a concern of the State, so also may its distribution Even assuming a policy of high employment and high wages, there will still be need of an authority which can control those blocks and diversions of food traffic which in former times have often been so costly to the consumer Nowadays, moreover, we should deem our rulers negligent if they did not accumulate "buffer stocks"—of wheat and sugar for example—to smooth out the fluctuations due to gluts and shortages For some time to come, in fact, a bold policy of food control will still be required, which fits in with the HOME SECRETARY's assurance in last week's debate that "while shortages last and economic difficulties confront us the utmost efforts will be made by the Government to ensure that fair dealing as between one citizen and another shall still be secured by the State"

11 Lepinger, H Die hepatogenen Erkrankungen Berlin 1929; Adler A *Z ges exp Med* 1925 46 371
12 Baar H. S., Lloyd T W *Arch Dis Childh* 1943 18 1; *Ibid* p 124
13 Maizels M Paterson, J H *Lancet* 1940 ii 417
14 Marrack, J R. Food and Planning London 1942.

18 Le Gros Clark, J Food Controls of the Future *Food Manufacture* 1945 20 177 181 210.

Annotations

BENEVOLENCE AT CHRISTMAS

SOME people can wish others well, and act upon it, all the year round, but many of us find this Cheeryble standard of benevolence out of our class We all have our benevolent moments, however, and it is a good thing for us if one of these happens to coincide with the annual Christmas appeal of the Royal Medical Benevolent Fund, for then we have the satisfaction of knowing that our kindly impulses will be directed to good purpose The appeal published in another column this week from the new president of the Fund, Sir Arnold Lawson, is one that must impress us all

In an annual review of the Fund's work, Sir Arnold notes the rise in investments from £109,428 in 1927 to £307,248 in 1944, with a comparable rise in income Distribution has gone up from £11,916 in 1927 to £25,284 in 1944 Nowadays the administrators of the Fund set themselves a higher standard of relief than used to be possible they plan to give every case a minimum allowance of 30s a week after the rent has been paid Those who need special care and attention have been helped to meet the expenses of nursing-homes, and there is a project under consideration to provide a home or homes for old people who need residential care Medical students have responded well to an appeal for support, and old subscribers have remained loyal Letters from recipients of Christmas grants show as usual how imaginative it was to establish a custom which brings so much pleasure and ease to doctors and their kin who have fallen on evil days

THE REGISTERED DISABLED

SINCE the end of September the Ministry of Labour has been compiling the voluntary national register of disabled persons The final numbers on the register are expected to be in the neighbourhood of 2 million, with a wage-bill amounting to £300 million a year. These figures were quoted by Lord Rushcliffe, presiding at a conference on health and work arranged by the British Council for Rehabilitation on Oct 10

It is believed that most of the disabled on the register will be able to take jobs on equal terms with the fit, and, to make this possible, services are being provided under the Act to give these disabled men and women whatever physical or mental treatment or vocational training they need to fit them for work. Employers of 20 or more workers will be under a statutory obligation to fill vacancies with people on the register until they have reached the quota prescribed for their industry To reable these people thoroughly, doctors in charge of their treatment may need to keep an eye on them until they are settled in industry; and the industry should keep in touch with those who get injured until they are fit to return to work To help the Ministry of Labour, and to foster this joint interest, employers, workers, and doctors have been brought together on the National Advisory Council, under the chairmanship of Lord Ridley Local advisory committees on disablement, with panels of experts to advise them, have also been set up in some 270 places, and these will keep in touch with local industries employment exchanges, hospitals, welfare organisations, and voluntary bodies The local advisory committees are in touch with the Ministry through the disablement rehabilitation officer (DRO), whose task it is to shepherd the disabled man from the hospital back to the workshops PEP has criticised the present DROs,[1] but it is likely that, when there are more candidates, the type of man chosen will be better suited to the job.

It will be a skilled task to place each disabled worker in the right work; but, as a correspondent of the *Times* points out,[2] the difficulties will be lightened by the use of a new form drawn up by the Ministry of Labour with the help of experts from the Ministry of Health and Pensions This provides a means of analysing physical function in such a way that it can be interpreted in terms of working capacity The questions can be answered with a "yes" or a "no" by the examining doctor for example, can the man lift a weight of 20–56 lb, can he climb a ladder, can he work in extremes of hot and cold? Industry, the *Times* writer says, must now produce a counterpart form, showing what demands different jobs make on the worker.

1. See *Lancet*, Sept. 15, p 343 2 *Times*, Oct 10, p 5

NUTRITION IN ITALY

A RELATIVELY rapid method of assessing the nutrition of the inhabitants of a region must prove valuable in the coming months An UNRRA team, working in Italy under Dr. A. J. McQueeney and Dr J Metcoff, has shown that a fair estimate can be based on the examination of children and of pregnant and nursing women, since these are the people who suffer first and worst from food shortage. Speaking at UNRRA's London headquarters on Oct. 9, Dr Metcoff said that the team carried out 34 nutritional surveys, samples being drawn from among the poorest members of the population, the results therefore reflect not the average Italian nutrition, but nutrition at the lowest level Some 2500 children, and 600 pregnant or nursing mothers were examined in districts in and near Rome, eastward to Ravenna and Milan and southward as far as Pontecorvo The data from all these places showed that the nutrition of the children, judged by height and weight, fell roughly within the lower limits of the normal range for American children Some form of nutritional deficiency was evident in 31% of them, and in 90% of these the deficiency disease was rickets. The remaining 10% mostly had riboflavine and vitamin-A deficiencies Anæmia and gross malnutrition accounted for only 1–2%, indeed there were only 17 grossly malnourished infants in the whole survey, and these were all in institutions—either hospitals or orphanages. No evidence was found of either vitamin-B_1 deficiency or pellagra. Of the pregnant and nursing women 3 5% had classical nutritional deficiencies, mainly of riboflavine and vitamin A. There were only 4 cases of anæmia among them

The team, besides assessing the degree and extent of malnutrition as evidenced by clinical examination, and providing information for the use of UNRRA, was able to encourage Italian interest in the organisation of surveys and the treatment of malnutrition. A technical subcommittee which included the leading medical specialists was formed by the Italian government, and this body drafted a pamphlet on malnutrition which was sent to 20,000 doctors The pamphlet set out basic criteria for the diagnosis of malnutrition, and was accompanied by record cards on which detailed findings could be recorded. A notifying system, based on these records, has also been established, so that malnutrition is now in effect notifiable in Italy The criteria were proposed by the Italian subcommittee, and Metcoff thought it possible that in some respects they would not be fully acceptable to American or British physicians They included, for children, famine œdema, signs of pellagra, purpura, signs of rickets or scurvy, craniotabes, night blindness, keratomalacia, cheilosis, rhagades, spongy or bleeding gums, a red shiny tongue, or an atrophic tongue indented by the teeth, and any evidences of neuritis or beriberi. In the pregnant or nursing women the examiner is required to note the presence of family œdema, hypertrophied or bleeding gums, night-blindness, neuritis, and signs of endocrine imbalance and of tuberculosis, malaria, or syphilis Tuberculosis is on the increase, but this can be ascribed in part to factors other than malnutrition—to overcrowding, the breakdown of sanitation, the closing of sanatoriums, and the dissemination of infectious patients Rickets has always been common in Italy and there seems to be no evidence

that it has suddenly increased The Italian subcommittee has arranged, at five universities, refresher courses in pædiatrics for Italian doctors, and the Rome courses have already begun They last a fortnight and include 38 hours spent at lectures, and about an equal period spent in watching practical demonstrations and in visits Many Italian doctors have been out of touch with medical advances for some years, they have proved extremely keen and gave much support and help to the American team

ANILINE POISONING FROM MARKING-INK

NEARLY 60 years ago a curious outbreak of cyanosis among babies in London was traced to absorption of aniline from the marking ink used to mark their napkins The danger of using such napkins before they have been boiled or otherwise laundered seems to have been forgotten, because Graubarth and his colleagues of New Orleans[1] now report 17 cases of poisoning from this cause with 4 deaths, and they have collected nearly 40 reported instances of similar trouble Of 32 babies in the nursery at Touro Infirmary, 17 unexpectedly and gradually became cyanotic, with rapid and in some cases difficult breathing All of those affected were wearing unwashed napkins stamped with an aniline dye, whereas the remaining 15 were wearing old napkins. War time shortage, both of napkins and of staff, is blamed for the mishap although it might, out of ignorance, happen anywhere Other clinical manifestations included irritability, jaundice, loose stools, vomiting, hæmaturia, and in one instance an enlarged spleen Of those who survived none showed any evidence of cerebral damage and there was no report of any refractory anæmia Of the 4 deaths, 3 were in premature babies Differential diagnosis is concerned with other possible causes of cyanosis—congenital heart disease, enlarged thymus gland, pneumonia (especially that associated with the aspiration of foreign material), intracranial hæmorrhage, inhalation of coal gas, various drugs, and disinfectants all these were eliminated, and Graubarth made the diagnosis on the basis of a similar experience in Cincinnati in 1929 Treatment included the administration of methylene blue, gr ¼ with each feed for 2 days, and the use of oxygen with 5% of carbon dioxide Blood transfusions were given to 9 infants Neither oxygen nor methylene blue had any obvious effect Apart from the removal of the source of poisoning, transfusion of blood or red cells suspended in saline seems the most logical treatment The conclusion to be drawn from this accident is that all newly marked clothes must be laundered before being worn by babies, or indeed by anybody

EVOLUTION OF ANTIBIOTICS

IN his Lister lecture to the Royal College of Surgeons on Oct 11, Sir Howard Florey, FRS, reviewed the history of the use of micro-organisms for therapeutic purposes from Pasteur to penicillin He recalled that the term "antibiotic" was introduced by Vuillemin in 1889 to indicate an organism which was not a parasite but was strictly antagonistic towards the life of another organism, as a lion or a snake is antibiotic towards its prey Pasteur and Joubert in 1877 were the first to describe antibiosis affecting a pathogenic micro-organism when they showed that the rapid growth of the anthrax bacillus in urine can be stopped by addition of some common aerobic bacteria By adding such bacteria to a suspension of anthrax bacilli they made it harmless when injected into animals and these facts they said perhaps justify the highest hopes for therapeutics" In 1885 Bahes studied the mutual antagonism of different kinds of bacteria which he recognised might be due to definite chemical inhibitors, and he suggested that one kind might be used to cure an infection caused by another kind Cantani, in the same year, in the treatment of tuberculosis explored the idea of replacing one organism by another less harmful In 1887 Garre demonstrated on agar plates antagonism such as that between *Pseudomonas fluorescens* and *Staph aureus* and proved that it was not due merely to rapid growth of one organism at the expense of the other, but to a substance elaborated by one of the organisms and killing the other His technique and that of Doehle, said Sir Howard "differ little, if at all, from those employed by some workers at the present day" After discussing the attempted use of certain infections (such as erysipelas) to produce immunity against others more chronic (such as lupus) he described how in 1898 two Russians Honl and Bukovsky, treated infected ulcers with "proteins" from cultures of *Ps pyocyanea* In the following year Emmerich and Löw introduced the first antibacterial extract into medicine—namely pyocyanase, prepared from cultures of the same organism This was undoubtedly bactericidal and was given for many different diseases and by many routes, even intrathecally "It can be said with some truth that there is little that has been done with penicillin which was not attempted with the earlier antibiotic, so far as the means then available allowed" In 1898 Gosio produced a crystalline antibiotic, mycophenolic acid, from a mould

After recalling further work on related lines by Lode, Frost, and Nicolle; Vandremer's use of aspergillus extracts against the tubercle bacillus both experimentally and clinically and various forms of "replacement therapy," including Metchnikoff's advocacy of colonising the bowel with *B acidophilus* the lecturer reached the 1920 s, when some new ideas and procedures were introduced. Experimenters turned their attention to yeasts, actinomycetes, streptothrices, and spore forming organisms, and Dubos produced his tyrothricin Various antagonistic contaminants were noticed in cultures before 1929 when Fleming found that a contaminated mould had lysed a culture of staphylococcus, and obtained from the mould the active substance he called "penicillin" Yet another decade was to pass before penicillin was put on a practical basis in 1940 by the observations of the Oxford team, and only after 70 years of experiment on antibiotics did medicine find itself possessed of "an antiseptic beyond the dreams of Lister

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Sir JOHN ORR, MD, FRS, MP, is accompanying the British delegation to the United Nations Congress on Food and Agriculture in an advisory capacity

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"Every successive war has narrowed the margin of safety by which the species itself survives in the midst of the powers of destruction it has devised It is the aim of every belligerent during the war to break down not merely the material supports of the enemy's fighting power but the very cohesion of the society they sustain Experience all over Europe today shows that when hostilities end the forces of anarchy set in motion by war do not automatically cease to operate The engines of victorious power, which have been hitherto used to destroy have to be reversed and used constructively to re-establish society and government among the defeated But with every war there is more leeway to make up more effort required to overcome the disruptive tendencies before reconstruction proper can begin In their striving for victory the allies created in Germany such devastation as destruction of the foundations of society as industrial Europe has never known The proportion of their available strength that they must now devote to the mere cancelling out of what they themselves have done is prodigiously high The danger that there may ultimately be a war after which the [illegible] momentum of decay is so great to be balanced even by the entire strength of the victors—that is that the [illegible] towards a final collapse of civilisation will go on [illegible] formal war has ceased The instance of the atom [illegible] that this point would almost certainly be reached [illegible] ever again break out between the great Powers [illegible]

leading article in THE TIMES Oct 9 p 5

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[1] Graubarth J, Bloom C J, Coleman I C, Solomon H N J Amer med Ass 1945 128 1155

Reconstruction

HOSPITALS

MORE SURVEYS OF REGIONS

NONE too soon, though not too late, we are receiving the reports that should form the basis of future hospital services The first of the dozen area surveys undertaken by the Ministry of Health, or on its behalf by the Nuffield Provincial Hospitals Trust, described the state of affairs in London and the surrounding area.[1] This has since been supplemented by an independent report from the voluntary hospitals[2], so the data for London and its "hospital drainage area" are now reasonably complete Four other regional reports are reviewed below, and the pattern of thought of the surveyors is thus becoming apparent

These reports are not final, they represent the views of those who compiled them, not of the Ministry Hence there is much diversity in the plans proposed for each area—a diversity greater than can be explained merely by reference to geographical or sociological considerations This has at least the merit of enabling those who have the making of the final plans to test all and hold fast to that which is good. But the varying nomenclatures adopted certainly do not simplify comparisons

The London surveyors have rejected the conception of the key hospital, preferring a series of main or district hospitals, each with about 800 beds, serving a population of something between 100,000 and 200,000 The voluntary hospitals' report, on the other hand, is prepared to see the continuance of the general hospitals of 150–250 beds, staffed by part-time specialists, while developing 1000-bed key hospital teaching centres There is little doubt that the solution offered by the Ministry's surveyors is more likely to provide the higher quality of service for the hospital sick

The proposals for South Wales follow closely those for London District hospitals are called area hospitals, but, with this modification, the suggestions are interchangeable The Eastern area report reverts to the key hospital, with three main provincial hospitals (similar to area hospitals in size and function), and a number of county general hospitals of 100 or more beds. The Berks, Bucks, and Oxfordshire report adds further to the complications by supplementing area hospitals with hospital centres Northern Ireland reverts to key hospitals plus area hospitals, here termed provincial hospitals.

All reports condemn the cottage hospital as it stands today, but propose to incorporate it in future schemes as a centre for the minor sick, the normal maternity case, and the emergency At the same time, it must be linked with a major hospital, and must have a visiting consultant staff to reinforce its general practitioners where necessary.

On fever hospitals, there is all but unanimity against the small isolated unit and in favour of the special block at a larger hospital The exception is provided by the Eastern area report, whose authors still consider that the prime function of the fever hospital is isolation and the protection of the community

General recognition is given to the need for increased accommodation for institutional midwifery, though whether this should be at cottage hospitals or the larger area hospitals is disputed

In all the areas surveyed there is a deficiency of almost all types of bed, but matters are worst in South Wales and Northern Ireland New hospitals must have a high priority in our building plans, and the coming of a National Health Service which aims at providing the best for all must usher in a period of hospital building as vigorous as, and we may hope more æsthetically satisfying than, the late Victorian era

1 See *Lancet*, 1945, i, 600.
2 *Ibid*, Sept 15, pp 342 and 345; Sept. 22, p 377

South Wales and Monmouthshire

The second of the Ministry's surveys, prepared for the Welsh Board of Health, covers South Wales and Monmouthshire[3] Its authors were appointed by the Ministry, not by the Nuffield Provincial Hospitals Trust, and it is therefore more in line with the hospital survey of London and the surrounding area than with the next two surveys (both the work of Nuffield surveyors).

The South Wales area is exceptionally interesting from the point of view of hospital planning It is roughly triangular, with its apex to the north and its 90-mile base formed by the South Wales coastline The population, just short of 2 million in 1938, is concentrated in the south-east corner more than 80% live in Glamorgan and Monmouthshire. As a result, hospital planning has to meet the needs of communities ranging from crowded Swansea and Cardiff to sparsely populated mountain and agricultural areas. A further peculiarity is the presence of the mining valleys, each a one-industry community with a strong and lively local patriotism, often showing itself in a miners' hospital provided and controlled by its users The units of local government are smaller than in most parts of England, of 17 boroughs, 7 have a population of less than 5000, while of 48 urban districts 17 have populations of less than 2000.

Not only is the area inherently interesting, but the observations of the surveyors are acute They point out, for example, that the relatively satisfactory operating-theatres and radiological departments in most hospitals are associated with the popular appeal which these two specialties have for the general public, whereas other less spectacular special needs are neglected There is almost no aspect of hospital organisation—from record keeping to psychiatric departments—on which they have not something useful to say And their approach to the problem of hospital size, based on the necessity for segregation of special types of case into units of adequate size, has more than local value.

Three main types of hospital are proposed Small local or general-practitioner hospitals should cope with medical cases not requiring detailed investigation, normal maternity cases, some of the chronic sick, and some forms of infectious disease Area hospitals should be the main stay of the service, staffed by specialists but also providing local hospital services for the immediate vicinity. Certain area hospitals would provide individual highly specialised units and would be termed group hospitals Thus the proposals are virtually identical with those made in the London survey. A careful examination of the degree of segregation necessary for efficient work leads the surveyors to the conclusion that 500 beds is the best size for an area hospital In one or two cases, however, they have been forced to recommend much smaller area hospitals

Sparsely inhabited rural areas present a special problem The linkage between cottage and area hospitals must be even closer here than elsewhere, not only must some major emergency surgery be done locally (thus necessitating an overlapping surgical specialist service) but nursing staffs should be linked, so that physical isolation may be overcome by an interchange of staff

South Wales shows the usual multiplicity of hospital owning authorities, added to which its bed shortage is worse than elsewhere, while the proportion of obsolete accommodation is high In 1938 there were 7945 beds for purposes other than tuberculosis; the surveyors estimate that at least another 7000 are needed Maternity beds need to be increased from 340 to 930 But, in addition, no fewer than 4089 beds are in hospitals or parts of hospitals which are quite unfit for use Thus, in all South Wales needs something over 11,000 new hospital beds If this huge addition is to be made, detailed planning of the new hospitals becomes an urgent necessity, so that maximum utility is achieved Such a plan is presented in the report

South Wales is divided into 16 hospital areas, each determined by geographical and socio-economic factors Their needs are summarised in the following table.

It is clear that South Wales is a distressed area so far as hospital accommodation is concerned. Yet hospitals

3 Hospital Services of South Wales and Monmouthshire By A. Trevor Jones, MD, MRCP, DPH, Prof J A. Nixon, CMG, MD, FRCP, and Prof R M F Picken, MB, B SC, DPH. Welsh Board of Health, 1945. HM Stationery Office Pp. 120 5s

	Area sq miles	Mid 1938 population	No of area hospitals proposed	No of local hospitals proposed	No of new beds needed
Rural Monmouth	370	47 132	1	4	237
Newport	97	122 709	1 (g)	6	609
Monmouth—					
Eastern Valleys	45	92 270	1	2	307
Western Valleys	80	110 200	1	5	797
Brecon and Radnor	1035	42 907	1	2	186
Rhymney Valley	74	98 721	1	3	396
Cardiff	140	313 218	2 (both g)	6	2157
Taff and Cynon	140	144 217	2	3	594
Rhondda Valley	70	124 780	2	4	674
Ogmore	184	106,8*4	1	5	366
Avon and Neath	116	117 476	1	2	393
Swansea	219	242 480	2 (1 g)	4	1736
Llanelly	164	99 701	1	2	465
Carmarthen	751	69,554	1	3	413
Pembroke	610	75 805	1	5	362
Cardigan	839	62,870	2	3	334

g = group hospitals

require not merely wards and beds but also specialist medical and nursing staff It looks as though South Wales is going to need two or even three five-year plans to put things right

The Eastern Area

The survey of the Eastern area [4] is less comprehensive Furthermore, its authors (working for the Nuffield Trust) have adopted different and generally less rigorous criteria, and give less space to problems of communication and administration

The area covered includes Cambridge, Suffolk, Norfolk, the Isle of Ely, the Soke of Peterborough, and Huntingdon county, and its population is 1½ million. There are no great urban centres, and the administrative authorities are too many and too small As a result, specialist services are poorly developed : for example, in the whole area there are only four psychiatric beds, and only two hospitals with a psychiatrist on the staff !

Instead of the three types of hospital generally favoured, four types are proposed :

1 A key hospital for the whole region.
2 Three principal hospitals in the three main geographical divisions
3 A number of county general hospitals of 100 or more beds, each affiliated to a principal hospital
4 Local hospitals of under 100 beds, staffed by general practitioners, but with visiting consultants

These proposals are open to a number of familiar criticisms. To provide 3 5 acute beds per 1000 of population, an additional 1150 beds would be needed in the region as a whole The radium and X ray therapy facilities of the area are poor and urgent temporary action seems to be called for The surveyors hope that an adequate home midwifery service will encourage mothers to prefer domiciliary midwifery Certainly, the existing maternity accommodation is quite insufficient Of the treatment of infectious diseases the authors say : "The idea, prevalent in some quarters, that every isolation hospital should be large enough to have a resident medical officer, his own laboratory, &c., is contrary to experience" They favour the continuance of small isolation hospitals, but with some staff linkage All this is disappointing, especially when we find 28 beds each recommended for Peterborough and Hunts The survey however, shows up the black spots and brings together the data needed for a comprehensive plan for the Eastern area

Berks, Bucks, and Oxfordshire

The next survey [5] is another of those sponsored by the Nuffield Trust, and is again less rigorous than those of surveyors appointed by the Ministry It takes full account, however of geographical features, transport and the natural flow of patients and is well illustrated with maps. Furthermore, valuable subcommittee reports on the various specialist services are included

The region has two main centres (Oxford and Reading), and two subsidiary centres (Aylesbury and the Windsor-Slough conurbation). Its population is increasing rapidly and in 1938 was just over 850,000 Of its 75 hospitals, 41 have less than 50 beds. The only two hospitals with over 300 beds are at Reading and Oxford The pathological and orthopædic services of the area are comparatively well organised both on a regional basis, with Oxford and Reading as the two main centres.

The deficiency of beds is estimated at just under 3000, the present number being 5711, and there is a corresponding deficiency of medical personnel of consultant and specialist status

The most interesting proposal of the report is the recommendation that cottage hospitals should develop into health centres This cuts across the oft-expressed view that beds should not be available at health centres, but it makes use of the fact that many cottage hospitals are already foci of the health services in their districts. Furthermore they propose to embody a main general-practitioner health centre with the outpatient department of each main hospital This would certainly have an advantage in teaching hospitals, but whether it would be really helpful elsewhere is less certain

Comparisons between the different surveys are rendered difficult as a result of the varying terminologies adopted In the present report, four types of hospital are suggested

1 The teaching hospital (Oxford)
2. The area hospital (Reading Slough Windsor and Aylesbury)
3 The hospital centre (Banbury, Newbury, High Wycombe, and Maidenhead)
4 The rural health centre (with under 50 beds, at some 22 points in the region)

It is perhaps a pity that the Ministry of Health did not suggest a uniform terminology to the surveyors, before they started their tasks

Northern Ireland

The hospitals of Northern Ireland have been surveyed for the Nuffield Trust, and are described in a report to the Northern Ireland Regional Hospitals Council The population of Northern Ireland is about 1,500,000, with the main concentration at Belfast (469,000) and the rest of the province, Londonderry alone has more than 50,000 inhabitants. Thus the problem is primarily one of serving an agricultural community but, thanks to the existence of good motor roads, no village is more than three hours' journey from Belfast.

Once more, multiplicity of authorities presents a problem In 1938 there were no fewer than [illegible] officers of health for a population of 1½ [illegible] England, voluntary and municipal hospitals [illegible] alongside one another

The general scheme proposed is for a [illegible] located at Belfast, with medical schools [illegible] 8 "provincial" hospitals each of about [illegible] points staffed by specialists, and each [illegible] tion of about 100 000 In addition, there [illegible] tage hospitals staffed by general practitioners [illegible] with their appropriate provincial hospitals [illegible] consultants when necessary

In 1912, only 882 out of 10,641 [illegible] place in hospital ; in 1937, the corresponding [illegible] 2058 out of 9151 The province as a whole [illegible] state, lags far behind what is [illegible] should be provided at all provincial [illegible] obstetric specialists available [illegible] domiciliary work in case of [illegible] substituted for the treatment [illegible] hospitals.

Northern Ireland has a [illegible] death rate : in 1937 it was [illegible] 70 for England and 74 for [illegible] deaths take place in [illegible] more sanatorium beds [illegible] brought up to the level [illegible]

4 Hospital Services of the Eastern Area. By Sir William Savage, MD DPH Sir Claude Frankau, CBE MD BS, FRCS and Sir Ian H Gibson. Ministry of Health 1945 HM Stationery Office Pp. 54 2s 6d.

5 Hospital Services of Berkshire Buckinghamshire and Oxfordshire By Sir E. C. Beveridge, FRCS, Prof G. L. Gask, CBE DSO FRCS and Prof R. H Parry MD FRCP DPH. Ministry of Health 1945. HM Stationery Office Pp 97 5s

6. Survey of the Hospitals [illegible] Stanley Harvey [illegible] William MacArthur [illegible] MD FRCP [illegible]

A suggestion is made for the establishment at rural cottage hospitals of polyclinics Here should be housed the ante- and post-natal clinic, tuberculosis clinic, the midwife and district nurse, and a casualty department with a small theatre, as well as rooms for general medical and surgical outpatient work. In smaller villages, polyclinics without beds should be set up

A Belfast hospital centre is proposed, to be developed on the basis of the Royal Victoria, Royal Maternity, and Sick Children's Hospitals Here a 23-acre site offers ideal accommodation for dental, eye, ear, nose and throat, and orthopædic hospitals.

The administration proposed is based on regional advisory councils, with the retention of voluntary and municipal control of individual hospitals. In a reservation, Dr Duncan Leys opposes the perpetuation of two separate organisations, particularly in Belfast He is considerably more critical than is the main report "The services in Northern Ireland," he says, "lag so far behind other regions, which are themselves considered to have great deficiencies, that there is all the more reason why our recommendations should be radical" If Northern Ireland can "afford" less than other areas, then her resources must be supplemented from Imperial funds. Dr. Leys is also critical of the staffing proposals made for provincial hospitals; anything less than first-rate specialist staff must be rejected, and such staff must be paid for the work they do A note on hospital buildings by Dr. Stanley Barnes gives valuable practical hints to those concerned with new hospital construction.

The whole report is written clearly and concisely, with explanations where necessary, and it contains a section on terminology, to enable it to be understood by the non-medical reader

Special Articles

TRAINING FOR AMERICAN DOCTORS RELEASED FROM THE FORCES

THE American Medical Association has founded an information bureau for doctors leaving the Forces This has now published, from 535 North Dearborn Street, Chicago 10, an Information Bulletin for Medical Officers, which interprets the Serviceman's Readjustment Act of 1944, and describes the postgraduate opportunities offered

To qualify for financial aid from the Administrator of Veterans' Affairs, the "veteran" must have served 90 days or more, and if over 25 must show that his education was interrupted or impeded Those eligible are entitled to education or training, or to a refresher or retraining course lasting a year (or the equivalent of a year in continuous part-time study) At the end of a year's course, other than a refresher or retraining course, the veteran is allowed further courses depending on the time he spent in the Service after Sept 16, 1940 The total period of education or training may not exceed four years

He may attend any approved institution that will accept him, and may change his course of instruction if he has good reason; but if his progress is unsatisfactory his course can be terminated. The fees are paid, and if necessary the cost of books and equipment and other necessary expenses may be covered, up to a total payment of $500 for an ordinary school year. A veteran also gets a maintenance allowance, while on a course, amounting to $50 a month or $75 if he has a dependant He may, moreover, receive a loan to buy or repair his home or equip his practice.

Judging by 21,020 replies to a questionary already noticed in these columns (*Lancet* 1945, i, 695) it seems that 20% of doctors in the American Forces would like short refresher courses lasting less than six months, especially in medicine, surgery, general training, and obstetrics and gynæcology The medical schools and hospitals report that plenty of opportunities will be open to them. There are 718 civilian hospitals approved for internships in the United States, offering 8000 house-appointments Before the war the number of medical students graduating annually did not exceed 5500, but some held internships for two years at a time In the coming months appointments will be made for only one year, so there should be plenty of vacancies for veterans who wish to take such posts

Some 12,000 doctors have expressed a wish to take specialist courses of 6–36 months, and there are about 700 civilian hospitals approved to give such training. An increase in resident posts is being arranged.

The bureau has prepared summaries of information from the counties in the different States, to show the prospects for doctors entering practice. These give the population of the county and of the principal cities, and facts about miles of highways, telephone systems, housing, schools and universities, rents, and climate, the names and addresses of the officers of the county medical society, the numbers of hospitals and beds, the birth-rate, the number of doctors already in practice or retired, and the public-health facilities. The bulletin also includes a table showing which States accept the medical qualifications granted by other States This problem of reciprocities is one complication of medical practice which we are spared in the United Kingdom

Apart from these civilian preparations, plans are being made by the American Army to provide courses for the doctors who choose to stay in the Forces Fellowships, resident posts at Army hospitals, and specialist courses will be arranged, and those who have been doing administrative work during the war are to have the opportunity to return to clinical work and to qualify as specialists

THE VOLIMS PLAN

IN June, 1944, at the request of the chairman of the Consultant Services Committee of the three Royal Colleges and other consultant representative bodies, a general meeting was held, at the Royal College of Physicians, of the non-undergraduate teaching consultants of the metropolitan area This was confined to consultants attached to the 150 or more non-undergraduate teaching voluntary hospitals of London —i e, it excluded consultants attached to undergraduate teaching schools, and also those engaged whole-time in local-government service

After this meeting, a committee of 14 non-undergraduate teaching consultants of London was elected, with Mr. W. E Tanner as chairman and Dr T Rowland Hill as secretary, and this committee has since worked regularly to prepare a plan for a consultant and specialist service for the nation This plan, entitled *A Regional Consultant and Specialist Medical Service based on University Medical Centres*, was published recently, and has been widely circulated to consultants and others. Copies can be obtained from the secretary of the committee at 14, Wimpole Street, London, W1

In addition, this committee of non-undergraduate teaching consultants has three members on the Consultant Services Committee who play their part in expressing the opinions of the type of consultant they represent Not long ago it convened a general meeting of non-undergraduate teaching consultants in the London area to report to them, to present its plan to them for their comments, and to refresh itself generally with their present opinions The meeting unanimously approved the committee's plan. It also unanimously decided that coöperation between the committee and the lately-formed association of the major non-teaching voluntary hospitals should be as close as possible, and that as far as possible the same personnel should serve in the metropolitan area for the two bodies.

The committee is now known as the VOLIMS Committee, from the initial letters of Voluntary hospitals Of London Independent of Medical Schools

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THE 1945 volume of the BRITISH ENCYCLOPÆDIA OF MEDICAL PRACTICE and its cumulative supplement (Butterworth Pp 396 and 251 37s 6d together) can now be set beside their forerunners Medical progress is recorded under the main headings: critical surveys, drugs, and abstracts Among the eleven surveys this year, each by an authority in his subject, are articles on the rapidly growing subject of mental disease by R D Gillespie, tropical medicine by Sir Leonard Rogers, FRS, and diseases of the alimentary tract by the late Sir Arthur Hurst. Nearly 900 abstracts cover articles in British, American, Scandinavian, and Swiss journals, and it should soon be possible to review European journals thoroughly again The high standard of this useful series was set by the first editor, Sir Humphry Rolleston, whose death in September of last year was a grave blow to his associates in the work.

In England Now

A Running Commentary by Peripatetic Correspondents

WALKING into an office of our Control Commission in lermany I found a prominent notice

WARUM EINFACH MACHEN WENN ES KOMPLIZIERT GENAU SO GEHT?

hich may be freely rendered for those unfamiliar with loche as "Why simplify matters when you can do things he complicated way?" The official then occupying the oom could not identify the quotation, nor did he know ho put it up "We change rooms—and jobs for that natter—so quickly now," he said "It might have been nybody, but in the three days I've been here I've felt it aust have been a Very Senior Person with a sense of the ardonic" I am glad to say the official did not obey the ajunction on the wall but smoothed our path swiftly nd effectively

In the vast structure of British Bureaucracy there nay be some few officials who take that wall notice as heir guide because it gives them a greater sense of mportance, but there cannot be many for the anonymity of the Service and the well-defined hierarchy nilitate against it Any impelled to follow it by nalicious humour must be even fewer Some, it is true, nay choose the tortuous way because they don't know nough to come in out of the hail, but these are the small ry No, I think our officials who deliberately complicate natters are really astonishingly few This is not a videly held view perhaps, and when one is faced with an ncome tax form or a B—— of T—— circular there is a good deal of temptation to reverse the opinion But ne must remember the immense range of modern egislative activity—for which, of course, Parliament and ultimately the Man in the Street is responsible—and the olossal difficulty of framing a general regulation so that t covers *all* possible contingencies Of course, the proof s the pragmatic test The fighting men won the war, ut they had to have supplies and support, and no uman machine could have given them what they needed, r could tackle such a matter as the supply problems of he BAOR today, unless it was extremely efficient—and nd a sense of humour

* * *

Listening to the RAF symphony orchestra playing the verture to Verdi's *Force of Destiny* took me back to he performance of that great opera in Rome last spring What a scene was there! One associates the turning up of the lights between the acts with lovely women in gala dress, their shoulders bare, their jewels sparkling, and heir men folk standing behind them in sombre contrast Not so in May this year The lights went up to show an opera house packed with khaki Young men of every ank and every unit from every part of the Empire and he States, enthusiastically applauding A few civilians, heir women folk in afternoon dress, were scattered among the mass of military I was anti Gigli when it began He had only just been allowed back after being uspected of being too great a supporter of Mussolini, and n the first act he was not unlike Musso and was dressed in a costume such as he would have loved; this ncreased my resentment and it may explain his transient exclusion There was a sailor boy near me, a little midshipmite, who was an enthusiast for him; he had many of his records, and had seized the opportunity of a day in Rome to see and hear the man himself And so we settled down in friendly disagreement to enjoy the next scene in the great inn

Then the personality of the man and the voice began to grow on me He crept up to the other male singers; then he passed them He had with him a great soprano, a name forgotten for the moment, that in the future may rival Tetrazzini's, and finally he caught her up and passed her too At the end of the great scene in the monastery I leant across to the midshipmite and whispered, "I take back all I have said against Gigli."

Why do they not put on this opera in England? It is far better than Rigoletto, which deals with actions so foul that if any Englishman understood the plot he would never go and see it twice, whereas the story of the Force of Destiny, though sad, is dramatic with food for thought and of a high moral code The music is grand all through, without any tunes that can be hackneyed like the Duke's song in Rigoletto There are moreover two things in it of special interest One is an entry at dawn of a ragamuffin lot of tattered soldiers singing a slow marching song at a shuffle It has nothing to do with the movement of the drama, but is introduced merely for its beauty Why did not we encore it as we did all the great songs of the soloists? For is not this a solo sung by a chorus? The other is the opening chords of the overture I would venture to put them up against those of any other composers outside Beethoven and Sibelius

* * *

They came, at first a few and then a drove the Æsculapiads of the New World to succour wartorn Europe Khaki-clad and with British names and customs they shared our clubs, our meetings, and our fireides. Up sprang their hospitals almost overnight clean wards and messrooms, well-ordered stores, theatres, and pharmacies. In their laboratories were shiny benches, virgin glassware, and crystal-clear solutions. Smart white-gaitered sentries "checked in" from their white-painted control offices In the motor pool stood strange high monsters of the road, regimented for war and errands of mercy There were libraries, cinemas, and baseball grounds, as well as cosy bars with lantern lights iced fruit cocktails, and exotic wall paintings They shared out parcels from home in their warm Nissen huts and put up on the stark concave walls photographs of their far away families Off plain deal tables they ate prefabricated steaks and Maryland chickens with apricot jam They poured out sweetcorn from cans and treated us to large fruity ices and hot chocolate sauce There was pride in their handicraft, as their chapels showed, for only their best would do Everywhere efficiency and quality, with sufficient of everything for the job in hand Then came the convoys and their jobs began The sterilisers steamed, the X ray plants hummed, and the centrifuges roared The purple dressing-gowns of the convalescents made their welcome appearance as blood, penicillin, and faith in the future speeded them back to their units.

The months passed and we got to know them—colonels, doctors, nurses, and enlisted men. Many were the meetings and the consultations They treated our men and we treated theirs They came to learn, youths of a young nation, but they taught us much They transformed our sleepy towns into energetic schools of medicine In leisure hours they swarmed our country lanes on bicycles and in rare bouts of sunshine played with our children on the greens, giving them candies and peanuts Some married our daughters and our sons. They loved our ancient churches and studied the flowers in our meadows They had aunts to visit, ancestral homes to photograph, and souvenirs to seek The aroma of strange tobacco pervaded our streets Hospitable and witty, they were the possessors of good manners and good teeth They tolerated good humouredly our lack of central heating and culinary understanding, and enjoyed above all the humble cup of tea in the family circle They told us of their homes and we wrote to their families Strange world that they who speak our language, share our jokes and ancestry, and fight the same battle against disease should be reckoned foreigners to us and we foreigners to them Citizens of the same world, we must needs be in separate sovereign States and perhaps willy nilly be required to serve separate interests

They went as quickly as they came for the lightning has severed the chains of bondage The hospital trains have ceased to run The wounded are healed and have left for home The hospital cities are dismantled and the men in the Nissen huts have packed their books, souvenirs, and photos and filed off to the ports in their fantastic trucks The bulldozers have levelled the last dump of empty cans and all is still. There is dust on the empty shelves of the pharmacy, the little trim gardens are overgrown, and the white sentry box is empty Now, only the miniature house is inhabited which the mess sergeants built for the tomtits The abandoned huts sadden our eyes as we recall friendships fashioned in the hinterland of war The stimulus of their presence is now a memory, for three thousand miles and a disordered world economy, separates us from them truly our cousins And our lazy old town has lapsed into dreams again.

But they will write and remember us And we shall not forget them

PS—I wish we had a cosy bar in our ho

Parliament

ON THE FLOOR OF THE HOUSE

MEDICUS M P

THE serious business of this first session of the Labour Government of 1945 has begun A Bill to enable necessary controls, including control of prices and of distribution, has passed its second reading without a division It is only challenged by the Opposition to the extent that they say it should not endure for more than two years, and the Government have decided it must endure for at least five years A Bill has been introduced to bring the Bank of England under public control—and the reaction in the City is a rise in Bank shares, presumably because the proposed compensation payment to the shareholders for their holdings is regarded as favourable The first instalment of the Government's massive programme of Social Security legislation has passed its second reading, and there is promise of the rest early in 1946. Demobilisation has been speeded up, including the demobilisation of doctors Mr Bevin has reported on the dislocation of the Foreign Secretary's Conference, but he believes that things can yet be put right

Faced with the complex business of getting Europe's economic affairs into some sort of order before winter, and the problems arising from the liquidation of Japanese rule in the Far East, Parliament is working like a controlled dynamo, and its assemblies are quieter and less tempestuous than can easily be believed

The discussion on controls was technical rather than politically controversial Again in the discussion on the Industrial Injuries Bill, one speaker after another showed a detailed grasp of social conditions Many of the speeches were maidens—and very good maidens, knowledgeable, restrained, and well expressed This is going to be a workmanlike Parliament, more given to economic discussion than ordinary party politics

The conference of the Food and Agriculture Organisation of the United Nations—which arose out of discussions at Hot Springs—opened at Quebec on Oct 16 And Sir John Orr, MD, FRS, MP, is acting as the Government's scientific adviser About the end of October there is to be a full-dress debate on the conditions facing Continental Europe this winter

Much work is going on in preparation for the presentation of the Government's proposals for a National Health Service Discussions with the medical profession and others concerned must continue But the practical building up of the GP strength in the country by demobilisation from the Services has an A1 priority at this time, and it looks as if the plans for extending the medical services in our factories, our hospitals, and our homes will demand a bigger annual intake of students into the medical profession

The relation between the National Health Service in this country and the Colonial Medical Service may perhaps become closer And what is to be the future of the medical services of the Navy, the Army, and the Air Force, which must inevitably be of greater size than those of the regular forces before 1939 ?

FROM THE PRESS GALLERY

Compensation for Industrial Injuries

On Oct 10 and 11 the House of Commons considered the National Insurance (Industrial Injuries) Bill, third of the four Bills necessary to give effect to a comprehensive social insurance system Mr J. GRIFFITHS, Minister of National Insurance, in moving the second reading, said the scheme was based on insurance against risk and not on liability for compensation By and large, everyone employed under contract of service or apprenticeship would become insurable without income limit, and several classes of people not necessarily covered by contract of service, such as taxi-drivers, were also included The essential difference in this Bill from the present Workmen's Compensation Acts was that benefits would be related to the degree of disability and not to loss of earning power

The Government proposed that the basic rate for injury benefit for 100% disablement should be 45s and the worker could also claim an addition of 25% if he could show that by reason of his injury he was no longer able to follow his previous occupation or an occupation of equivalent standard. Benefit lasted for six months from the date of the accident, unless the injured man could start work before that time and asked to be assessed for pension Pensions would be awarded in proportion to the degree of disablement and irrespective of a worker's earnings

The whole scheme had been framed with the war pensions scheme in mind, and in making the regulations the Ministry of National Insurance would be influenced by the schedule of assessment used by the Ministry of Pensions, but they would not necessarily be bound by it. Extra benefits would be provided for severe cases. For instance, if a man was rendered virtually unemployable by his injury—i.e. if he was unable to earn more than £52 a year—and was likely to remain so, he could ask for an additional allowance of £1 a week. An additional allowance up to £1 a week might also be paid if constant attendance was needed, even if the necessary care was given by the injured worker's wife If a pensioner had to enter hospital for further treatment he would, while in hospital, receive pension at the 100% rate, irrespective of his normal assessment There would, however, be a reduction of 10s. a week in respect of home savings and an attendance allowance would cease for that period The Bill also made provision for dependants

Assessments for pension would be made by medical boards consisting of at least two doctors, though for minor cases of temporary disability a single doctor might sit if the claimant agreed. Medical appeal tribunals would deal with cases in which the injured man disputed his assessment, and disputes about the allowances of child dependants would come under the appeal machinery already provided in the Family Allowances Act

The Bill also provides for financial assistance to be given to those engaged on research into the causes and prevention of industrial accident and disease and for the Minister himself to employ people to carry out such research The accident-rate in this country was still appalling, Mr Griffiths affirmed, and he was desperately anxious to see the position improved He commended the Bill to the House, not only for its cash benefits, but also as the foundation upon which a great constructive human service could be built

Mr. OSBERT PEAKE compared the Bill in its importance and scope with Mr Lloyd George's National Insurance Act of 1911, and promised that there would be no danger to its passage from the Opposition, indeed, he suggested, most of the critics were now to be found inside the ranks of the supporters of the Government. Mr CLEMENT DAVIES, speaking from the Liberal benches, however, was disappointed with the Bill. It was an improvement, but he would have liked the Government to produce a broader, wiser measure, bringing in all members of the community

Other speakers on the Government side of the House, closely acquainted with workmen's compensation administration from the trade-union point of view, suggested that the benefits proposed did not sufficiently take into account that for the first time the workman was contributing to his own compensation. Some injured men, it was argued, would get less benefit from the new scheme than they might have expected under the existing law

PROTECTION OF HEALTH WORKERS

Mr. R CLITHEROW, a final-year medical student, appealed to the Minister to include health workers who contracted tuberculosis through being directly in contact with tuberculous patients in the course of their normal duties or within some reasonable time afterwards. The Liverpool corporation hospitals committee, of which he is a member, were distressed, he said, to see the number of nurses who contracted tuberculosis They felt this responsibility keenly because they had X-ray photographs of nurses, and their full medical reports before they started, and the girls had gone down with the disease perhaps in two years Counsel's opinion had been sought and the committee had been advised that tuberculosis was not an industrial disease

Dr. STEPHEN TAYLOR pointed out that the Bill perpetuated the distinction between industrial injury and disease Sickness benefits should be raised to the same

level as those applying to workmen's compensation under this Bill Once that had been done, all the difficulties arising from the phrase "or in the course of employment" and the schedule of industrial diseases would disappear He hoped that the Minister would assure the House that nurses would be covered, particularly those doing private nursing With every safeguard the nurse was still liable to certain pathogenic infections, to whitlows and septic fingers kidney affections and septicæmia, but unfortunately every precaution was not always taken in many hospitals Regular X rays, Mantoux tests, and blood-counts were not done He was convinced that nurses were more liable to tuberculosis than the rest of the community, although that was disputed Hitherto trade unions had had to waste their energy getting diseases scheduled when that energy should have been used in getting rid of the diseases The Minister was taking power to promote and assist research into the causes, incidence and methods of prevention of industrial disease, and Dr Taylor hoped that he would include research into the methods of treatment of industrial accidents and disabilities, because such treatment especially of minor accidents, was still far from perfect More publicity should be given to the results of research Between the two wars much good work was done by the Industrial Health Research Board, but it had remained locked up in rather dull reports instead of being applied to industry Mental disability, he continued, made up a large part of industrial disability, and while the barbarian concentrated his neurotics, the civilised person compensated them, and, even more important rehabilitated them That was no easy job, and he hoped the Minister would generously finance research into industrial psychiatry

Dr H B MORGAN regarded the Bill with misgiving For the last 25 to 30 years workmen's compensation had been his life and he saw no reason why workmen's compensation should be brought in as part of a general social insurance scheme It was a special phase of life demanding special legislation He objected to the whole procedure by which the benefit was not related to the man's rate of earning, and he was terrified of appeal tribunals, with a commissioner and perhaps a medical assistant

Dr BARNETT STROSS found certain principles in the Bill attractive compared with the somewhat unprincipled state of affairs that existed today Speaking as a medical man he was glad that there should be complete dissociation between compensation and earnings, for the people who had been penalised in the past had been those whose earnings had been low, and the penalty had passed inevitably from the breadwinner to his wife and children, so that they had helped to form a class of people vulnerable through sickness and malnutrition to every type of disease

Mr G S LINDGREN, parliamentary secretary to the Ministry of National Insurance replying to the debate, said there were great difficulties in the way of making special provision for health workers within workmen's compensation, because of the incidence of the diseases with which they dealt, and the lack of proof that diseases arose out of, or in the course of, their employment The Minister would desire, if possible, to provide for them, and he would like to have discussions with the Ministry of Health, and those who could speak on behalf of the workers concerned, to see whether it was possible to bring them in

Increased Old-Age Pensions

Mr GRIFFITHS announced that the Government intend substantially to improve the basic rates of old age pensions to be paid on retirement and so to reduce the need for supplementation Proposals to this end, which will also include improvements in the rates of a number of other national insurance benefits will be contained in the Bill which it is hoped to introduce early next year and to pass into law during the present session Special arrangements would be made to bring the pensions provisions for existing classes of old age pensioners who had retired, including widow pensioners over 60, into operation at a date substantially earlier than that at which it would be possible to operate the scheme as a whole

QUESTION TIME

Demobilisation of Medical Students

Replying to a question Mr G A ISAACS Minister of Labour, said that students eligible for release from the Services in Class B included students in medicine dentistry, and veterinary surgery recommended by their universities or the appropriate schools who either (1) gave up their reservation to join the Forces or (2) joined the Forces before the present conditions of reservation were in operation, but would have been reserved if they had been in force Only men in release groups 1–40 (i.e with substantially three years service) are eligible

Replying to a further question Mr J J LAWSON, Secretary of State for War, said he regretted that he could not grant extra leave to men in the BAOR to sit for postgraduate examinations Men in the BAOR were eligible for 12 days leave approximately every six months and those who wish to sit for an examination might apply to have their leave advanced or retarded to suit the examination

Medical Man-Power

Sir JOHN MELLOR asked the Minister of Labour whether he was aware that in August the BLA had 1 medical officer for 409 officers and other ranks, compared with 1 general practitioner for 2570 civilians in the United Kingdom; and what steps he had taken to correct this anomaly —Mr A. BEVAN, the Minister of Health who replied, said the answer to the first part of the question is yes The civilian position can only be remedied by an acceleration in the rate at which doctors are released from the Services, and the Government are at present urgently considering to what extent this is practicable.

Special Diets for Invalids

Mr D L. LIPSON asked the Minister of Food if he was aware that under existing regulations sufferers from diabetes and tuberculosis were unable to obtain the eggs which their doctors had prescribed for them; and if he would issue fresh regulations giving more consideration to the diets recommended to patients by their own doctors.

Sir B SMITH replied: I am advised that the present allowances of foodstuffs for diabetic and tuberculous patients are adequate for their needs I could only allow them extra eggs at the expense of other members of the community some of whom are suffering from complaints for which eggs are a necessity, and I should not feel justified in doing this during the present general shortage of foodstuffs

Experimental Health Centres

Mr C. W DUMPLETON asked the Minister of Health whether pending the establishment of a National Health Service, he would initiate experimental health centres in suitable places so that valuable experience could be gained.—Mr BEVAN replied: I do not think it would be practicable to make this provision in advance of the new legislation. But I am pressing on rapidly with the preparation of the Health Services Bill which will deal fully with the subject.

Medical Practices

Mr C. YORK asked the Minister of Health (1) if he would state the Government's intentions in regard to compensation for medical practices if taken over under the National Health Service, and (2) whether he could announce the policy of the Government in regard to medical practices, in order that demobilised doctors might decide whether to purchase practices.—Mr BEVAN replied I have this matter under immediate review I am not yet ready to make any statement, but I know the urgency and I will do so as soon as I can.

Need for Tuberculosis Nurses

Flight Lieutenant F BESWICK asked the Minister of Health how many tuberculous sufferers were now awaiting admission into sanatoria and how many beds it was estimated would become available if the required hospital staff could be found.—Mr BEVAN replied The number of patients awaiting admission to sanatoria is about 5000 Above 1600 existing tuberculosis beds are closed for lack of staff; and a sufficiency of additional accommodation could be provided without much difficulty if staff for it were available

RAF Demobilisation

In an answer to Sir G Fox, Mr J Strachey Under Secretary of State for Air, stated that in general releases in November and December for the RAF would reach group 23 but there would be some exceptions For me the age-and-service group reached would be

Letters to the Editor

AN APPEAL FOR CHRISTMAS

SIR,—It is my privilege this year to ask you to submit to your readers the Christmas Gifts appeal which for so many years has been issued by the late Sir Thomas Barlow and so generously supported by the medical press

The Christmas Gifts appeal has a special significance this year, for, although peace has come, the material blessings which peace is supposed to bring are as yet merely dreams without substance Food is monotonous and scarce, fuel is terribly short and its cost fantastic, clothing and prices generally are on the same high level, and even for those in fairly comfortable circumstances the outlook for the festive season is distinctly drab. Inevitably the burden of high prices and shortage falls most heavily on the poor, and for them there will be little money for celebrations of any sort this coming Christmas

Last year there was collected a record sum of £1817, which was distributed as follows: 483 of our people each received a Christmas Gift of £3 at a cost of £1449; in addition we were able to give 184 of our poorest a further sum of £2 each as a New Year's gift, costing £368

I feel that we must, if possible, do at least as much as last year, and indeed I am pleading for another record If, for instance, subscriptions amounted to £2000, we should be able to give everybody a Christmas Gift of £4, and there would still be sufficient over to give some of the poorest an extra £1. Is it too much to ask? A very generous profession has already done so much, but my excuse is the hard times which still lie ahead Believe me, the gratitude these gifts evoke is very great and often extremely moving

Donations may be sent (marked "Christmas Gifts") to the Secretary of the RMBF, who will gratefully acknowledge them

Royal Medical Benevolent Fund,
1, Balliol House, Manor Fields,
Putney SW15

ARNOLD LAWSON,
President.

HYPOPIESIA

SIR,—Perusal of Sir Maurice Cassidy's rejoinder to my letter surprises in his abrupt dismissal of symptom-producing hypotension as a "blood-pressure neurosis," and disappoints in the apparent bankruptcy of all idea on his part of any remedy. Presumably Sir Maurice believes that symptomatic hypotension exists only in the imagination of patient and doctor, so needs no treatment It would be right to say that, amongst medical men, all the points he makes are common knowledge and an old story Much of his letter is critically destructive, which doubtless he feels justifiably so, though it is just possible that his attitude towards the hypopietic may be wrong.

Apart from the commonly associated neurasthenia shown by the hypotensive patient, his appearance and his several subjective symptoms indicate low blood-pressures, and in my view are distinctive enough, circulatory mostly, never referable to the heart itself, and only needing confirmation by instrument To withhold from the sufferer all information about his low-pressure readings does not rid him of these symptoms, which do in reality exist in some hypopietics though clearly not in all, most probably occurring with temporary falls in pressure Does Sir Maurice deny that they happen at all, only to ignore them, is reassurance the full measure of the treatment he would offer? If so, there is cold comfort for the hypotensive subject who appeals to him for advice and guidance.

To label hypopiesia merely a neurosis is to scoff at the patient for his complaints, to be blind to his symptoms, and to do literally nothing for him, so seems to me rather more likely to "perpetuate," not the admitted neurotic element, but the disorder with all its discomforts

Bournemouth S WATSON SMITH

SIR,—I fear that not many cardiologists will agree with Sir Maurice Cassidy that hypopiesia is not an abnormal condition. After lowering the systolic pressure we found a decrease in cardiac output, impairment of renal function, &c. (Harris and Platt, *Lancet*, 1931, ii, 629) Indeed this type of patient frequently complains of dizziness, loss of energy, &c. The neurosis in these cases may possibly have a physical basis Their end-results are of interest Judging by my experience, which, however, is limited, hypotension predisposes to cerebral disease Possibly some neurologist will tell us whether cerebral thrombosis is frequent in this condition I have often seen hypotension turning into hypertension. It is clear that if a satisfactory method were available this condition ought to be treated

Liverpool I HARRIS.

SIR,—Sir Maurice Cassidy criticised the letter of Dr Watson Smith "in order not to perpetuate" the opinion of a distinguished physician which he considers wrong. For the same reason I feel compelled to object to the opinion expressed by Sir Maurice

Our time—which is full of worries, fears, and dangers—can be regarded as a mass experiment in proof of my doctrine that arteriosclerosis develops from arterio-atony, and that it does not represent a disease sui generis but is the means of healing the damage caused in the atonic arteries As to the arterio-atony, it represents only a part of the general atony, whatever may be its cause, as I have always held (*Lancet* 1932, i, 385) Arterio-atony is a state in which the subsequent development of the sclerosis can be forestalled by adequate treatment

Watson Smith in his letter gives the full classical description of general atony, but errs when he regards the hypopiesia as the cause rather than as a consequence. In Sir Maurice's opinion it is a "a widespread delusion that a pressure of 120 in a subject of forty to fifty is pathological and that in an individual of any age pressure of or below 110 calls for alarm and despondency" He maintains that "systolic pressures as low as 100 can and should be disregarded, and that on no account should the patient's symptoms be attributed to them"

I think that Sir Maurice's doctrine, if followed, may be detrimental not only for the present but for the future fate of the patient It may be that he shares the general opinion which regards high pressure as an alarming symptom In my experience low pressure statistically involves more dangers and more serious complications than high blood-pressure I am thinking here especially of the dangers of thrombosis and embolism, cramps, &c In this point I believe every observant practitioner will agree with me

If hypopiesia is commoner today than in previous decades the cause can easily be found in our disturbed times, and therefore the mass appearance must be psychogenic The fact that atony mostly represents a "neurosis" does not entitle us to minimise its significance or to disregard its treatment. If Dr. Watson Smith has seen but little success from galenic treatment, I sadly agree with him Other and more effective methods are tonics, like arsenic, different vitamins, and hydro-, climato-, and thalasso- therapies may help, but a strong warning must be sounded against violent exercise which may suddenly increase the blood-pressure whereby the sluggish arterial wall with impaired resistance may be over-distended and injured The arteries thus damaged later become sclerotic

I would not like to think so little of the application of the elastic belt recommended by Dr Watson Smith as Sir Maurice Cassidy does The belt may help the weakened circulation by supporting the abdominal wall. Because of the psychological origin of the hypopiesia, we may expect the greatest benefit from psychological treatment A good drink, a good cigar, or a cup of strong coffee to eliminate the inhibitions of the tired brain, a trip in cheerful company, a gay show or some Hollywood nonsense, to distract the patient from his sorrows and worries, but most of all a holiday should be advised in the old Roman sense of *otium*, full occupation of the patient by his hobby, by something different from his usual pursuits

London, W1 J. PLESCH

THE "PERFECT AP"

SIR,—Dr. George Day writes in your issue of Oct that it came as a new idea to those present when, in 1935, Jacobeus reported to the Tuberculosis Association that with a person lying on his side the lower lung does more work than the upper lung As a matter of fact Mr. Cortlandt MacMahon made this observation during

the 1914–18 war He reported it in an article on Gunshot Wounds and other Affections of the Chest published in *The Lancet* (1919, i, 607) In a subsequent letter (1920, i, 834) he wrote "I therefore always advise patients with an empyema to lie on the back, as described, or on the side where the rib has been resected, both from the drainage point of view *and for expansion of the lung*" (italics mine) Those of us who know Mr MacMahon's work have always given him the credit for this original observation

London W1 GEOFFREY EVANS

GAS-GANGRENE

SIR,—We have read with great interest Dr A H T Robb-Smith's article in your issue of Sept 22 on the tissue changes induced by *Cl welchii* type A filtrates In this field our work has been essentially concerned with observations on the effects of these toxins on the lipid elements of a number of body tissues and fluids (*Lancet*, 1945, i, 457, 487), which forms a part of a more extensive investigation into the etiology of fat-embolism which is now nearing completion

The first sentence of the last paragraph of Dr Robb Smith's article might be thought to indicate that we attributed fat-embolism in guineapigs and rabbits, following injection of *Cl. welchii* toxin, to the splitting of lipoprotein complexes in the plasma This is not the case In fact, we have presented evidence showing the improbability of this origin of the embolic fat in these animals Later in this paragraph Dr Robb-Smith refers to the occurrence and significance of fat-embolism in human cases of gas-gangrene The dangers of confusing post-mortem changes of fat distribution with fat-embolism are, of course, obvious In all our animal experiments extensive control groups were investigated and autopsy was carried out immediately In our human cases autopsy was performed at the earliest possible moment (in one case, uncomplicated by fracture, within two hours of death) there were no local signs of fat displacement by gas formation, nor was there evidence of any extensive breakdown of blood lipoprotein complexes The associated changes in the lung were compatible with the conception that the fat was embolic We concluded, therefore, that fat-embolism had occurred in our animals, and in the human cases we were able to investigate

We agree with Dr Robb-Smith that fat-embolism is probably only a contributory factor in the fatal outcome in cases of gas gangrene We were not able, however, to conclude from our limited number of cases what part fat-embolism might play in the production of the systemic reaction We have regarded this particular variety of fat-embolism more as an index of the dispersal of a number of tissue breakdown products than as a separate entity Because of this, and other observations, we suggested in our paper (1945, i, 487) "that products of tissue breakdown may be a more important factor in the systemic reaction than circulating toxin"—a view expressed independently at the same time by Macfarlane and MacLennan

A C FRAZER A D T GOVAN
Birmingham J J ELKES W T COOKE

SULPHATHIAZOLE IN IMPETIGO

SIR,—I was much interested to see the figures published by Brigadier MacKenna and Captain Cooper-Willis in your issue of Sept 22 My own experience in treating several hundred cases of impetigo entirely supports their conclusions.

In 1942 microcrystalline sulphathiazole (15%) was issued to commando troops to be used as a wound prophylactic At that time we had a number of troublesome cases of impetigo in the unit, and I misapprehended one tube of this preparation as an experimental remedy It proved far superior to any other I had tried, but as it was in short supply I did not feel justified in continuing to use it for this purpose, and I tried ordinary sulphathiazole instead The results were almost as good, and I have used the treatment exclusively ever since, both at home and abroad The time required for cure has rarely exceeded a week.

From the practical standpoint the treatment has been easy to apply One tablet of sulphathiazole of standard strength is made into a paste with some boiled water from the MI room sterilizer Crusts are cleaned off, and the paste is applied to the lesions and allowed to dry No covering is used This procedure is carried out twice a day for a couple of days, and thereafter once a day until weeping has ceased (usually the fourth day), after which the scabs are not removed but raw areas are "touched up" daily with a little of the paste The scabs come off in from five to seven days leaving the area healed

I have probably been lucky, but so far I have seen no case of sensitisation

BRIAN LEES

LUMBAGO AND SCIATICA

SIR,—While everyone must admire any coördinated efforts to throw light on the cause of such disabling affections as lumbago, I should like, as an intermittent sufferer, to sound a note of caution to enthusiasts ready to accept a single cause for this common ailment

Dr Cyriax does not give any diagnostic criteria for his hypothesis of abnormality of a low lumbar inter vertebral disk, except to say that radiology is of no use He describes "agonisingly painful coughing" as a well-attested sign of intraspinal lesions Apart from the word "agonising," which is almost pathognomonic of the hysteric, one can think of several other well attested causes of pain in the back on coughing

What would influence me chiefly against so simple a hypothesis as he puts forward is the fact that the lumbar region is not the only seat of "rheumatic" pain Bad as have been my attacks of lumbago, I have had worse attacks of intercostal pain, a painful joint or two, and frequent stiff necks since childhood Still, such disabilities are not crippling After relative immobilisation of the painful muscles by strapping, with citrates and citric acid and occasional purges, I am much better than I was 20 years ago—even for lawn tennis.

I should like to recommend to some enterprising editor a collection of articles entitled "The successful treatment of illness in ourselves," to be contributed by patients who are also doctors.

Broadstairs. MARTIN O RAVEN

HEALTH CENTRES

SIR,—Attempts at constructive discussion on health centres are frequently handicapped by the very varied, and often very nebulous, mental picture different people have of what each means by a health centre For this reason illustrated articles, such as the one you published last week, are to be welcomed and I hope this article will be followed whenever possible by other suggestions of designs for possible centres This present plan however, can hardly be regarded as the last word in health-centre design, even if it is only meant as a temporary centre As a matter of experience, temporary structures have an awkward habit of acquiring permanence, and it would be unwise to accept lower standards of building and equipment for them merely because they are intended to be temporary Nor must it be forgotten that it will be upon the first centres built or adapted that the judgment both of the doctors and of their patients will be given as to the desirability of this new form of practice This makes it doubly important not to begin with any scamped or ill conceived design

This present design, examined with these principles in mind, appears at once too extravagant and too scamped It is extravagant (as you have already pointed out) in its use of land and yet scamped in the accommodation it provides for each doctor and his patients

The centre seems to be designed to combine the public health provision of child welfare maternity, and dental services with that of a general practitioner service employing at least 12 and possibly 16 doctors X-ray, physiotherapy, and rehabilitation sections are also provided Such a centre could not unreasonably be expected to serve an urban population of some 30 000 people Indeed, it would not be economically possible to suggest at present such extensive provision for an appreciably smaller community Yet the suggested layout requires a site of approximately 450 × 200 ft and few towns now could afford to supply so large a site for a health centre in a position sufficiently central to be reasonably accessible to all the patients for whom it is intended

When we come to examine the sketch plan for the unit of doctors consulting rooms we find that little has been

done to provide either patient or doctor with comfort or convenience beyond that customarily available already in most doctor's own premises Each doctor is given a room, which (including a small curtained dressing cubicle and an alcove with a wash-basin) has the overall dimensions of 18 × 12 ft Windows are on one side only, and there is a single door opening on to a corridor The patients of four doctors have to share a single waiting-room measuring 12 × 12 ft This is not even centrally placed, but is reached from the far end of the corridor by a passage, 6 ft long, which passes the single lavatory provided for the use of these patients The overcrowding, inconvenience, and chaos this could cause on a busy winter's day can well be imagined Nor has anything been done to help to make efficient medical work easier, to save the doctor from unnecessary time-wastage, or to enable him to make the best use of the secretarial and nursing help that must be made available

Reference back, however, to some of the articles mentioned in your annotation, shows that much architectural thought has already been given to what might be called the public-health health centre In particular the article on health centres in the United States (1944, i, 131) gives welcome proof that even government plans for such buildings can be so designed as to allow easily of simple variations to suit local requirements But architects do not seem yet to have published designs that really help us to visualise the different types of general-practitioner health centre, suitable for different localities, which the country may soon be asked to provide and in which we may be asked to practice If THE LANCET could inspire the active coöperation of doctors and architects in the preparation and publication of suitable health-centre designs for our study and criticism, a very helpful step might be taken towards making the health centre a practicable and an acceptable possibility

Bromley, Kent A TALBOT ROGERS

A COMPREHENSIVE TRAINING COURSE FOR NURSES

SIR,—The city council of Plymouth has recently received the approval of the General Nursing Council to a proposal to establish a comprehensive training scheme for nurses, including the three municipal hospitals—namely, the City General Hospital, the City Isolation Hospital, and the Mount Gold Orthopædic and Tuberculosis Hospital Student nurses in training will spend a portion of their time at each of these hospitals and the periods will be as follows

After 8 weeks at the preliminary training school
- 12 months at the City (General) Hospital
- 6 months at the Isolation Hospital
- 6 months at Mount Gold Orthopædic Hospital
- 3 months at Mount Gold Pulmonary Tuberculosis Hospital
- 12 months at the City (General) Hospital.

The total period of the course would be 4 years, the last 6 months of which would be spent upon elective work including (*a*) maternity, (*b*) public-health clinics, (*c*) mental, (*d*) hospital X-ray department or theatre, (*e*) staff nurse or charge nurse at one of the above hospitals

The city council had under consideration the training of student nurses and the staffing difficulties of hospitals, and have come to the conclusion that the most promising method of improvement of the staffing position is to make nurses' training as attractive as possible While it is appreciated that a certain number of intending students may, in the early stages of the scheme, be deterred by the prospect of having to spend a proportion of their time at an isolation hospital and tuberculosis hospital, it is confidently felt that once the scheme has been in operation some time, and the added advantages in the way of more extensive training are appreciated, any reluctance will be overcome Existing students will be given the option of entering the new scheme so far as they are able to, or continuing on the present lines

The city council has also decided to appoint, at a salary of £600–£700 a director of training who must hold the sister tutor's certificate and have had experience in teaching, and who will be responsible for organising and coördinating all training and for stimulating recruitment of student nurses A further application to the General Nursing Council and Tuberculosis Association that the time spent at a special hospital in this course should be allowed to count towards the time required for the State-registered nurse subsequently to train for a special certificate, has not yet been approved

Plymouth T PEIRSON, Medical Officer of Health.

MEDICAL ASPECTS OF BELSEN

SIR,—I have just seen Lieut.-Colonel Lipscomb's article in your issue of Sept 8 With the greater part of his conclusions I am in entire agreement, but there are two points I would like to raise

Lieut.-Colonel Lipscomb very rightly says that the greatest care should be exercised in intravenous therapy in cases of starvation I think that he might have been even more emphatic and particular In the report submitted by Major E. M. Griffin and me, we pointed out that in autopsies on cases of starvation at Belsen the weight of the heart was in general between 110 and 250 grammes instead of the normal male 350 to 400 g or female 300 to 350 g. I think the conclusion to be drawn from this is that the capacity of the circulation might—very nearly must—be held to be of one-third to one-half normal capacity Personally I do not think too much emphasis can be given to this concept, in view of the imminent return of our own men in a similar starved condition from the prison camps in the Far East The moral is that the circulation of a starved person is much less adaptable and of far less capacity than that of a normal. Many of us are used to treating hæmorrhage and shock under war-time conditions We must drastically modify our ideas when we come to intravenous therapy in the starved

The other point that I wish to take up is in regard to the ten RAMC personnel who developed a fever which clinically resembled modified typhus On all these men I performed agglutination reactions whilst they were under treatment in the British wing Some I was able to follow for two and three weeks. With O strains of proteus at my disposal as antigen, I could at no time find any significant titre or rise of titre in these cases. Unless Lieut.-Colonel Lipscomb has obtained further serological evidence on these cases, I take liberty to suggest that a firm diagnosis of typhus is not established.

4 Mobile Bacteriological Laboratory BAOR A P. PRIOR.

RELEASE OF PHARMACISTS

SIR,—If the Ministry of Labour waits inactive while events drift to a crisis, it is quite probable that people will be unable to get the medicine prescribed for them during the coming winter

Briefly, the situation is that more than 300 pharmacists are needed to fill existing vacancies The need is not a question of guesswork, it represents the number notified from all parts of the country to the Pharmaceutical War Committee specially appointed to advise the Government on how available pharmacists ought to be allocated between civilians and the Services The largest number of special releases which the Ministry appears likely to concede is 100—an inadequate allotment

It is true that 400 pharmacists are to be released under "age and length of service" before the end of the year, but these men will be free to go wherever they like Only a few of them will be available for the vacancies which must be filled if a breakdown in the medicine supply is to be averted Many of the vacancies are in neighbourhoods, such as remote country places or the East End of London, to which a demobilised man will refuse to go when he is free to choose

Obviously it is in the general interest of the community to maintain a service essential to the health of the community as a whole If the Ministry of Labour refuses to maintain it, the responsibility is on them, but it does seem odd that they should ignore the unbiased advice of a committee of professional men and representatives of the Service departments set up by the Government to give it

London, WC1 JAMES C YOUNG, Chairman, Central Pharmaceutical Committee

Obituary

ERNEST WARD

MA, MD CAMB, FRCS

Ernest Ward had a cheerful self-confidence, a gift of expression, and exceptional drive—a combination of qualities that may be rather overpowering But in him they were associated with a humour and a diversity of interests which kept him human. But for two major illnesses, early and late in his career, he might have achieved more Yet he achieved much, especially in the work against tuberculosis to which he gave most of his life and he will long be remembered by many sorts of people

Henry Wylie

He was born in 1877 at Garforth, near Leeds where his father, Sir John Ward, was later lord mayor Educated privately and in Switzerland, he became a scholar of Clare College, Cambridge, and took a first-class in both parts of the natural sciences tripos Thence he went on to the London Hospital, and qualified, at rather a late age in 1903 As a resident he was exceptionally keen and energetic, and he was known to subsequent generations of London Hospital men through his lively contributions to their gazette In 1906 he took his surgical fellowship, but decided to be a general practitioner and entered a partnership at Llanelly, where he was surgeon to a steel works and to the local hospital From Llanelly, having married in 1910, he moved to Stockton on Tees as surgical member of another firm and at this time he was hon secretary of the General Practitioners' Association for Collective Research The special knowledge of tuberculosis which he afterwards displayed was first obtained at the Queen Alexandra Sanatorium at Davos, where he served as an assistant medical officer, and on his return to England early in the last war he settled at Paignton and became a whole time tuberculosis officer for Devon

Besides the work of a tuberculosis officer in a large county area, which he carried out with great energy and zeal, Ward found time for many outside activities. He served a term of office as president of the Society of Medical Officers of Health, and for many years was the mainstay of the tuberculosis subcommittee of the society, which took care of the interests of tuberculosis officers He was also the first secretary of the Joint Tuberculosis Council, and the Council owed much in its early days to his indefatigable pioneer efforts and breadth of vision, which included the organisation of the transatlantic tour in 1930 when some fifty doctors from this country paid a visit to the sanatoria of Canada and the United States He was also a versatile writer and had a journalist's eye for a situation Perhaps his best known work is *Medical Adventure* a book of essays on a variety of medical subjects including legal adventures as an expert witness, sidelights on the old club practice and one good murder story told with dramatic instinct On similarly variegated lines he contributed to *The Lancet* series, 'Grains and Scruples,' in 1937 Other works included translations of Lejar's *Urgent Surgery* (1915) and Broca's *Ligations and Amputations* (1917) From early days he had written frequently for medical journals, and on tuberculosis he wrote with sound sense and often with great effect as in his notable paper on conjugal tuberculosis published in these columns in 1919

In a pre-war age when medical writers ran to words in a way nowadays discouraged he used to advise students to skip the first column about Hippocrates and start halfway down the second But one never skipped Ward; he was always interesting and to the point His essay on encephalitis lethargica will surely rank as a classic among descriptions of diseases written by doctor patients It was compiled with complete detachment and accurate observation during the illness which left him with parkinsonian symptoms and compelled his retirement in 1941

Ward was a keen ornithologist and a botanist as befitted a man who had Dartmoor for his parish "Of all hobbies" he wrote, "natural history best befits the training and daily life of a doctor" His son has followed him in medicine

ROBERT CUNYNGHAM BROWN

CBE, MD DURH

Cunyngham Brown, who died on Oct 7, was one whom to meet was to remember, and to know was to love Son of a Scots minister, he was born in 1867 and educated at Glasgow and Durham After a few years of general practice his interest in neuropathology led him to Frankfurt, where he worked with Prof Carl Weigert, and subsequently to the National Hospital for the Paralysed and Epileptic

In 1899 he joined the Prison Medical Services, and in 1911 his specialist and administrative abilities were recognised by his appointment as deputy commissioner in lunacy for Scotland In 1915 he was seconded to the Army as officer commanding the Springburn Woodside Military Hospital. In 1916 he went to Macedonia with the 37th General Hospital, attached to the Royal Serbian Army There he established most friendly relations with the Serbs, by whom he was made Officer of the Order of St Sava, and to whom his commanding handsome presence made instant appeal, while his charm smoothed away difficulties He left this post to become medical specialist to the Salonika Command, and later returned to England for work with the Ministry of National Service

In 1919 he was transferred to the enlarged and reconstituted medical services of the Ministry of Pensions as deputy director general of medical services, and in 1920 he was appointed CBE *He held that post until 1925* when for health reasons he retired for a while from public work. His influence at the Ministry of Pensions is not to be measured by the short length of his service there "C B" became and remains a tradition Direct and uncompromising in his endeavour towards what he thought right, he had a way with him so that, as one of his colleagues wrote, 'you loved him most when most you disagreed" As an able administrator, as a specialist with breadth of vision and common sense, as a man embodying the humanities he left an enduring mark Of his occasional absentmindedness tales will long be told

From 1929 to 1932 he returned to active work as a commissioner of the Board of Control, and in 1936 he was commissioned by the Secretary of State for the Colonies to advise and report on the care and treatment of lunacy in Nigeria and neighbouring localities During the late war he was welcomed back to the Ministry of Pensions as a specialist on medical boards

His interests were not limited to his profession He delighted in sailing and in country life, and in conversation there were few subjects on which he did not reveal unexpected knowledge and insight Advancing years left him unchanged, and, despite recent family tragedies he remained young, charming, and gracious to the end

A S

WILLIAM STEWART McDOUGALL

MB EDIN

Dr W S McDougall was born in 1866 at Appin Argyllshire where his father of the same name was the minister From school in Aberdeen he was sent to Edinburgh University and graduated in 1889 Of his two practices the first was at Tongue in Sutherland and the second at Wallington in Surrey, where for nearly fifty years he showed his patients how much a doctor can offer besides medicine

'Times changed Wallington village became a senior suburb, and the suburb became a target area. 'Dr Mac (as he was inevitably called) raced a long succession of cars round the local corners; he sat up late reading journals and books of every kind from Wild West to philosophy or listening to the midnight news and even at 70 he seemed perfectly at home in a mechanised world at war Yet he remained essentially a countryman Continuing the favourite

pursuit of his childhood, he was a beautiful fisherman, and he accumulated a vast collection of fishing books, as well as many on flowers and animals and birds. More important, however, he kept a countryman's scale of values His behaviour to everyone was consistently matter-of-fact, unperturbed, and friendly, and the confidence he inspired as a doctor owed as much to his character as to his clinical talent, his carefulness, and his long experience of human vicissitudes He could understand weaknesses he did not share, the reassurance he brought was based on power to control himself as well as others, and he himself, however ill, was always 'very well thank you'

"As father, grandfather, uncle, and cousin—all in a biggish way—his home was the meeting-place of a large 'connexion,' and his hospitality was in the best Highland tradition He wanted always to make his guest easy and content, and he had this same attitude towards his patients But the kindness of his hospitality, conversation, or advice had none of the exaggeration that sometimes lessens the charm of Celtic sympathy He was indeed often silent, and seldom spoke at length, he might even seem rather detached. and he was never insincere With his wide range of humour, including the sardonic, he can have had few illusions about his fellows, but he probably saw more of their best side than most of us do, and of the living, as of the dead, he preferred to say nothing unless it could be good

"Having apparently no sense of his own superiority, he was well placed as senior partner of a large firm of practitioners, and with persistent courage he continued his work throughout the war till it was far beyond his strength But in his 80th year his hair was still dark and his attitude contemporary Neither fatigue nor age altered his personality, and he went on treating his neighbour better than himself"

Dr McDougall was consulting physician to the Carshalton War Memorial Hospital and a member of its original staff He married, first, Margaret Mitchell, of Ribigill, near Tongue, by whom he had three sons and two daughters, and secondly S H Mitchell, who survives him One of his younger sisters was the late Dr Mary McDougall of Croydon He died at Wallington on Sept 29

JAMES MACDONALD TROUP

M A ST.AND, M B CAMB

Dr Troup, who died on July 31 in his 78th year, was a Scotsman who made South Africa his home, and came to be regarded in Pretoria, where he practised for 43 years, as the ideal family physician He was born at Huntley, Aberdeenshire, the youngest son of the Rev Robert Troup, and was educated at Madras College and the University of St Andrews, where he took his MA In 1886 he went with a Guthrie scholarship to Cambridge and read medicine and mathematics He was a brilliant mathematician and in the tripos of 1890 was Seventh Wrangler He did his clinical work at King's College Hospital, where he was a senior scholar and became house-surgeon to Watson Cheyne In 1897 he went to South Africa to take up an appointment at Grahamstown, and after practising for a time at Somerset East he settled in Pretoria in 1902

Possessing an astonishing clinical acumen with a naturally inquiring mind, Troup might well have been a consultant physician, but he preferred the wider scope of general practice He liked nothing better than to be the adviser and counsellor of a multitude of families in and about Pretoria, but he never failed to keep pace with advances in medicine, being an assiduous reader of medical journals all his medical life A colleague, writing in the *South African Medical Journal*, recalls that his interest never flagged "when confronted with something obscure or unusual his tenacity of purpose would invariably find the solution—and this with very little help from mechanical aids In therapeutics, as in diagnosis, he was supreme" Dr A Pijper, the pathologist, writes in the same journal of his first meeting with Troup They had been in consultation over a patient and were standing in the street when Troup began to discuss an article Pijper had lately published on the diffraction of light by red-blood cells "He quietly explained where he thought I had gone wrong in my mathematics and physics, and we ended by sitting on the running-board of his car and drawing figures in the sand" Pijper also asks how many people realise that but for Troup tick-bite fever would probably still be unrecognised. By the early 1920's Troup had realised that this was a disease sui generis, peculiar to South Africa, he had worked out its clinical features and knew it was spread by a bite; but he left it to Pijper to elucidate its aetiology. In 1931 they described this mild tick-typhus, with "no mortality, no sequelæ, almost no complications, and practically no literature" in THE LANCET (1931, ii, 1183). As an anæsthetist Troup kept almost entirely to chloroform and ether, and his technical skill showed itself particularly in his administrations to children and the aged

Dr Troup married twice His first wife, Ethel MacDonald, died six years after he settled in Pretoria In 1909 he married Alberta Davis

Public Health

QUALIFICATIONS

REVISION of the course and examination for the diploma in public health has long been promised, and the General Medical Council are now considering a report by the Society of Medical Officers of Health which proposes a new syllabus [1] This is designed for the years in which a National Health Service is taking shape.

The new DPH course, as set out in the report, will omit practical training in chemistry, physics, physiology, biochemistry, and bacteriology, since the time hitherto spent on acquiring laboratory technique in these subjects could be more profitably used. For similar reasons practical tests in food inspection are to be left out.

To ensure that the candidate pays attention to practical demonstrations during his course, he will be required to keep, and produce at his examination, a day-book in which he is to discuss the implication of his practical studies He is also to write a dissertation on some subject he has encountered during these studies.

To provide a basic training in preventive and social medicine for all doctors taking part in the public-health services, the report suggests a postgraduate course lasting one academic term of whole-time study or the equivalent (300 hours) in part-time study At the end of this basic course a certificate will be awarded Those seeking a full qualification in public health will take a further course lasting two terms, or the equivalent, to fit them for the post of medical officer of health On passing the examination they will receive the DPH

The basic course is to cover the history of public health, functions of central and local authorities and voluntary bodies, agencies for relief, statistical information, control of infection, housing, physical education, heredity, health education and international health organisations Practical work will include demonstrations, visits, and exercises in epidemiological problems and the preparation of statistics

The course for the full qualification in public health will include the study of physiology, biochemistry, food and nutrition in relation to public health, bacteriology, parasitology, and medical entomology, as applied to epidemiology, mass aspects of disease, sanitation, water-supply, housing, town-planning; statistics, plans, administrative methods, the public-health laws, mental health services, occupational health, and health education. Candidates will live for four weeks in a fever hospital, or attend for 3 months part-time, and will undertake practical work in a health department

In addition, the report deals with the position of public health specialists, and recommends that doctors now in the service should be placed on the specialist register if they have had 5 years' postgraduate training and experience in the practice of medicine, of which not less than 2 have been spent in a public-health department doing work comparable with that of a medical officer of health and if they hold an approved academic qualification in public health

For newcomers to the service the criteria for admission to the register should be residence for not less than 12 months in approved hospitals or institutions, and not less than 6 months

1 Postgraduate Education of Medical Practitioners in Public Health. Report by a subcommittee of the Society of Medical Officers of Health, with Prof R. M F Picken as chairman Obtainable from the society at Tavistock House (South), Tavistock Square, London, WC1

general practice; training and service, for 2 years whole one 3 years part-time, in the central office of department the MOH of an approved authority, and a recognised academic qualification in public health

A second part of the report considers the training of officers and specialists who give service of a special kind the public health department These include child health officers, school medical officers, maternity officers, chest physicians engaged in tuberculosis work, and specialists in infectious diseases or venereal diseases It is suggested that in addition to taking the basic course they should have special experience in their subject, and hold a recognised qualification in it

Thus child health officers (including school medical officers) would be required to have had 18 months general clinical experience in resident medical and surgical appointments and general practice a year of special experience as a resident in a hospital with children's wards; and not less than a year in the child welfare section of a health department They would be expected to take a postgraduate qualification in child health the examination for which should give prominence to preventive and social factors.

Maternity officers, who in the subcommittee's view, should be responsible for the antenatal, intranatal and postnatal care of the mother, would be required to have the same general clinical experience as child health officers followed by two years experience in maternity hospitals or hospitals with maternity wards, and in clinics Some part of this time should preferably be spent in a hospital taking gynaecological cases and children. They should also attend antenatal, postnatal and child welfare clinics and should take a postgraduate qualification in obstetrics and gynaecology

Similar standards are proposed for the other specialists in this group, except that these—specialising in tuberculosis, infectious diseases, and venereal diseases—would be required to take a higher qualification in medicine instead of a special diploma

Infectious Disease in England and Wales

WEEK ENDED OCT 6

Notifications—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1683; whooping-cough 900; diphtheria, 479; paratyphoid, 11; typhoid, 15 measles (excluding rubella), 307; pneumonia (primary or influenzal), 377, puerperal pyrexia, 155, cerebrospinal fever, 38; poliomyelitis, 20, polio-encephalitis, 0; encephalitis lethargica, 0; dysentery, 207; ophthalmia neonatorum 70 No case of cholera or typhus was notified during the week

The number of service and civilian sick in the Infectious Hospitals of the London County Council on Sept 26 was 1021 During the previous week the following cases were admitted: scarlet fever 69; diphtheria, 41 measles 4; whooping-cough 11

Deaths—In 120 great towns there were no deaths from puerperal fever, measles or scarlet fever, 4 (1) from whooping-cough, 12 (1) from diphtheria 47 (7) from diarrhœa and enteritis under two years, and 8 (0) from influenza The figures in parentheses are those for London itself

Liverpool reported 10 deaths from diarrhœa and enteritis.

The number of stillbirths notified during the week was 30 (corresponding to a rate of 29 per thousand total births), including 11 in London

On Active Service

AWARDS

CBE

Colonel F A. BEARN, DSO MC, MD MANC, RAMC
Brigadier ERNEST BULMER, OBE, MD EDIN FRCP, RAMC
Brigadier J T McCONKEY, LRCPI, RAMC

OBE

Surgeon Lieut -Commander J S GUEST, RANR

For great skill and devotion to duty as PMO of HMAS *Australia* during the landing on Tarakan Island on May 1 1945

DSO

Lieut -Colonel M W GOWIN, MBCS, RAMC

MENTIONED IN DISPATCHES

Surgeon Lieut -Commander W H MILROY RANR

Notes and News

NURSES FOR THE TUBERCULOUS

IN view of the acute shortage of nurses in sanatoriums the Minister of Health asks all hospital authorities to consider whether they can release some of their trained or assistant nurses—who, of course must be willing to make the transfer—for training at such institutions If most hospitals can spare one or two nurses for this purpose the situation in the sanatoriums will be greatly eased On May 1 of this year the number of tuberculous nurses needed was estimated at 1909 (24 2% of the full establishment); in February the deficit had been only 1771 (23 2%) and in November 1944, 1471 (20 2%) Patients awaiting admission to hospital have risen from 4628 in March of this year to 4972 in June; so the situation is deteriorating The Minister asks that matron or other responsible officers will explain to their nurses how urgent the need has become He also asks as many hospitals as possible to make arrangements for nurses taking general or fever training to be seconded to sanatoriums for part of their training

PROHIBITION OF OPIUM

THE *Times* of Oct 10 announces that the British military administration has totally prohibited opium in Malaya and all British protected territories in the Far East. Before the war government revenue from the opium monopoly was being gradually reduced, with total prohibition as the ultimate aim. It is emphasised that the success of the new policy will depend on effective control of opium production in other countries, and the British Government are consulting other governments to secure their coöperation.

University of Cambridge

The title of the degree of MB, B CHIR has been conferred on the following: I M S. Chappel P J Coopo, M. E. P Hole, J E. Kellin L. A. Norris, H. M Russell, C N Smith J Whitham and G B. Wrong

Royal College of Surgeons of England

On Oct. 11 Sir Howard Florey, FRS, professor of pathology in the University of Oxford delivered the Lister lecture on the use of micro-organisms for therapeutic purposes (see p 503). Afterwards Sir Alfred Webb-Johnson, president of the college presented him with the Lister medal and prize of £500 Sir Howard, in returning thanks reiterated that the successful use of penicillin was the outcome of the work not of himself alone, but of a host of collaborators.

At a meeting of the council held on Oct 11, with Sir Alfred Webb-Johnson, the president in the chair, a Leverhulme research scholarship was awarded to Mr P B Ascroft for research on the pathology of head injuries

A diploma of fellowship was granted to David Barrett Feather (Leeds), and diplomas of membership were granted to the following:

C H de Boer Lucy M Dunkerley R L Greenwood, E. C Hutchinson, P M Jeavons H A Lane W H Lonsdale and Harold Wainstead

The following diplomas were granted jointly with the Royal College of Physicians of London:

D Phys Med.—J F Bach and L. J Crisp

DCH—H I C Balfour Henry Blair Agnes A Brash, E. H Brown E. F B Cadman Alexander Comfort, Nancy D Cox J G Dathan H L. J S Derham Glenys M M Donaldson F R M Elgood Elizabeth de C Falle I W Gallant Susanna Gordon Mona Griffin, G H. Griffith Ursula Jerram Alexander Kalan Margaret Kemsley Vivien G Lutwyche, Helen M C Morley Joan E. Neak G F Paget, Margaret Purdoe H E. Parry P L. Polani Phyllis Poyser Wall L. S Prasad H. J I Pugh, Mary M L Rutter Vivian M N Osborne D E. Narrow S S Yudkin Charles Zahra Neumann Hedwig L Zondek

Major (Non-Teaching) Voluntary Hospitals Staff

The annual general meeting of the Association of the Honorary Staffs of the Major (Non teaching) Voluntary Hospitals of England and Wales will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London WC2 on Friday Nov 9 at 2.15 PM. Mr H. J McCurrich is president of the association Mr Kenneth Heritage treasurer and Mr M P Reddington hon. secretary

Return to Practice

The Central Medical War Committee announces that the following have resumed civilian practice:

Mr F d Abren FRCS, 8a Harley Street, W1
Mr Geoffrey H Bateman, FRCS, 35 Harley Street W1
Dr J W Jacobson, TD, Wimpole Street W1
Dr G L. S Konstam, FRCP 40 Harley Street W1
Dr V H O'Connor 8 Lewin Terrace Leamington Spa
Dr W R Revell FRCS 87 Harley Street London W1

London Association of the Medical Women's Federation

On Friday, Oct 26, at 8 30 PM, at BMA House, Tavistock Square, WC1, Dr Beryl Harding will give her presidential address on relief work in Greece

Medico-legal Society

At a meeting of the society at 26, Portland Place, London, W1, on Thursday, Oct 25, at 8 15 PM, Dr W Norwood East will deliver his presidential address on society and the criminal

The Title "Nurse"

Since Oct 15 it has become an offence, punishable by fines, for persons to use the title of nurse unless they are State registered nurses or enrolled assistant nurses The Ministry of Health announcement that this regulation was to be enforced recalled that the Nursing Acts, 1943, make exceptions in favour of children's nurses, and of titles such as "trained nurse," "maternity nurse," "student nurse," "pupil assistant nurse" and others

Problems of Resettlement

Members of the Civil Resettlement Planning Headquarters at Hatfield will give four lectures on this subject at 26, Portland Place, London, W1, at 6 30 PM on the four Tuesdays of November Lieut.-Colonel A T M Wilson, RAMC, will speak on psychological aspects of resettlement (Nov 6), Major H Bridger, RA, on resettlement and the social worker (Nov 13), Chief Commander M B Boyle, ATS, on the social background of resettlement case work (Nov 20), and Lieut-Colonel Wilson, on some experiences in resettlement (Nov 27) Tickets may be obtained in advance from the organising secretary of the British Federation of Social Workers, 5, Victoria Street, SW1

Heberden Society

The inaugural general meeting of the year will be held on Nov 2 at the rehabilitation unit of the Royal Free Hospital, Gray's Inn Road, WC1, at 4 PM, when there will be an exhibition of relief-map modelling as a form of occupation therapy, photographic studies of the hand in arthritis, rest splints in 'Perspex,' a captured German metal-seeking apparatus, and a mobile physiotherapy cabinet At 4 45 PM there will be a lecture demonstration on recent advances in physical methods, when Dr C B Heald will demonstrate aerosols in rheumatism, and the aerophore and lumbago, Flight-Lieutenant B C Elliott diathermy without screening, radar apparatus modified for medical application, the balanced pulse generator and weak muscles, and an improved ultraviolet efficiency tester, and Dr Graham Weddell electromyography and fibrositis The inaugural dinner will be held at 7 45 the same evening at the Euston Hotel At 10 AM on Saturday, Nov 3, at the Middlesex Hospital, Prof B W Windeyer will lecture on the treatment of ankylosing spondylitis by X rays Tickets may be had from Miss Bereton, 91, Priory Road, West Hampstead, NW6 Doctors attending the postgraduate course of the Empire Rheumatism Council will be welcome at both meetings if they apply for tickets.

British Orthopædic Association

The annual meeting of the association will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, WC2, on Oct 26 and 27 On Friday, the 26th, at 10 AM, Prof T P McMurray will speak on Thomas and his splint, and Mr C H. Cullen on the infection of gunshot wounds with actinomyces. At 11 10 AM Mr St J, D Buxton will deliver his presidential address on the prevention of accident and limitation of injury, and afterwards Prof. H. J Seddon will describe Another Island Epidemic of Poliomyelitis. At the afternoon session, beginning at 2 PM, the following papers will be read Prof J Leveuf, primitive congenital subluxation of the hip, Mr J S Batchelor, congenital dislocation of the hip, Mr E W Buntcliffe, pollicisation of the index finger for traumatic amputation of the thumb At 4 10 PM Mr P G Hennell will give a lecture demonstration on clinical photography The dinner of the association will be held in the hall of Lincoln's Inn at 7 on the same evening On Saturday, the 27th, at 9 30 AM, Squadron Leader E. Somerville will speak on air arthrography of the knee joint, and Prof Harry Platt on the place of orthopædics in medical education and in the regional hospital service. At 11 10 AM there will be a symposium on methods of treatment of simple extra articular fractures of the femur, when the opening speakers will be Mr R. G Pulvertaft, Major John Charnley, and Mr G R Fisk.

International Pharmaceutical Meeting

The first meeting of European pharmacists since the war being held in London next month on the invitation of the Pharmaceutical Society of Great Britain The members of the bureau of the Fédération Internationale Pharm who will attend are Dr E Høst Madsen (Copenhagen) president, Mr E Saville Peck (Cambridge) and Prof D Os (Groningen, Holland), vice-presidents, Dr T. Potjewijd (Winschoten, Holland), secretary, and Mr C Moye (Brussels), assistant secretary

Royal Society of Medicine

The section of odontology will meet at the Royal College of Surgeons, Lincoln's Inn Fields, London, WC2, at 6 30 on Monday, Oct 22, when Mrs Lilian Lindsay will deliver her presidential address on the London dentist of the 19th century Afterwards Mr Roland Hill will describe abnormal dentition in Nigerian natives and Sir Frank Colyer will give a demonstration in the odontological museum On Oct 23 at 5 PM, at 1, Wimpole Street, W1, Dr T Izod Bennett will give his presidential address to the section of medicine will speak on hypertension and the discussion will be opened by Major Clifford Wilson and Dr. Mary Lockett At the section of urology, on Oct 25, at 5 PM, Mr Wilfrid Adams will give his presidential address on uretero-colic union On Oct 26, at 3 PM, at the section of epidemiology and State medicine, Dr Melville Mackenzie will read a paper on trends in public-health work in the city and State of New York, Massachusetts, and in Georgia At 4 30 PM, on the same day at the section of disease in children, Prof Norman Capon will give his presidential address on the training of clinical teachers

Appointments

ALEXANDER, MARION C., MB BELF examining factory surgeon for Wiveliscombe, Somerset
ELLIS R W, MB LEEDS examining factory surgeon for Horsforth, Yorks
EVANS, W E F, MRCS, DA senior anæsthetist, West Middlesex County Hospital
MCKISSOCK, WYLIE, MB LOND, FRCS temp surgeon, National Hospital, Queen Square, London
MURRAY, W A, MD GLASG, DPH medical superintendent, Ea Fortune Sanatorium

Births, Marriages, and Deaths

BIRTHS

BAYLISS —On Oct 10, the wife of Dr R. I S Bayliss, of Tettenh Staffs—a son
BEALES —On Oct. 10, at Oldchurch, the wife of Mr Philip Beal FRCSE—a son
ELLIOT —On Oct. 1, at Rhyl, the wife of Lieut -Colonel J. Elliot, RAMC—a son
GRAY —On Oct 7, at Cambridge, the wife of Major Charles Gr RAMC—a daughter
HUGGETT —On Oct. 8, to Prof Esther Killick, MB, wife of Pr A St. G Huggett, MB—a daughter
KELLOCK —On Oct. 11, the wife of Lieutenant T D Kello RAMC (MEF)—a son
MADDEN —On Oct. 7, the wife of Dr J G Madden, of Tollesbu Essex—a son
MARSHALL.—On Oct 7, at Carshalton, Surrey, the wife of T S Marshall—a son
PRICE.—On Oct 7, at Clifton, the wife of Dr C H G Price—a s
SNOW —On Oct 9, the wife of Dr R H. B Snow, of Hadleig Suffolk—a son
WHITTERIDGE.—On Oct 8, at Oxford, the wife of Dr Da Whitteridge—a daughter.

MARRIAGES

KAVANAGH—LEROUX.—On Oct 6, at Crawley, Edward Kavana surgeon lieutenant RNVR, co Wexford, Ireland, to Blanc Léoni Leroux
SPENCER SMITH—WILLIAMSON —On Oct. 8, at Bexhill-on Sea, T Spencer Smith, captain RNS, to Olive Margaret Kath Williamson
WILLIAMSON—COOKE.—On Oct 6, at North Shields, Martin Williamson, MC, major RAMC, to Jean Cooke

DEATHS

ANDERSON —On Oct 12, at Keswick, William Dunlop Anders OBE, MB CAMB, aged 87
BROWN —On Oct 7, at Lymington, Hants, Robert Cunyn Brown, CBE, MD DURH
BOWEN-DAVIES —On Oct 7, at Gerrards Cross, William Bowden-Davies, MRCS, aged 74
GOLDSMITH —On Oct 9, at Lowestoft, Edmund Onslow Gold BA CAMB, MRCS, aged 53.
HARPER.—On Oct 3, at Leopoldville, Belgian Congo, Fran Margaret Harper, MB EDIN, DPH
MCMUNN —On Sept 15, James Robert McMunn, CB, CMG, major general late RAMC, retd, aged 79
MOSES —On Oct. 11, in London, David Assur Henry Moses MRCS
SMITH —On Oct 8, in Cheltenham, Lionel Fergus Smith, MB DUBL., late RAMC, retd, aged 73.
STORRS —On Oct 9, at Teddington, Reginald Storrs, LE lieut -colonel RAMC, aged 70.

PSYCHOLOGY IN MEDICINE *

MILLAIS CULPIN, M.D. LOND., F.R.C.S.
FORMERLY PROFESSOR OF MEDICAL INDUSTRIAL PSYCHOLOGY IN THE UNIVERSITY OF LONDON AT THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

THE position of psychology in medicine has undergone great changes in the last few years and is not yet stabilised. These changes can be understood only in the light of history, which allows current beliefs to be put in perspective. Much of the relevant history has been given by Greenwood and Smith (1934), Smith (1939), and, in its more clinical aspects, Culpin (1931, 1936). I propose to give a brief outline of this history and show its continuity with the present.

There have always been two schools of thought, represented at one time by mechanists and vitalists, at another by iatrophysicists and animists, by realists and nominalists, and now, let us say by some people who are not psychologists and by those who are. On the one side was a desire to account for all psychological states and processes, indeed life itself in terms of biochemical or biophysical mechanism; on the other was felt the need for some principle that shall give unity to the body, manifesting itself in bodily functioning and activity, in emotion and thought. Here belonged the *physis* of Hippocrates, of which the historian, A. J. Brock (1929), writes:

> "The physis is not secondary to the corpuscles, but a long way prior to and older than they . . . it is the physis which puts together the bodies of plants and animals by virtue of the faculties which it possesses. . . . And when they are born it provides for them by the use of, again, other faculties—one of affection and provision for offspring, one of companionship and friendship for kin."

It is from *physis* that we derive the word physiology, and the paradox emerges that only some physiologists would grant the need for the conception of that physis of which they are nominally the exponents.

GALEN'S TEMPERAMENTS

Galen leaned towards animism, believing that "there is the creative power of nature that shapes parts according to the disposition of the mind." But he also produced a theory of temperaments, which guided medicine for many centuries and has given us a terminology the mechanistic purport of which tends to be forgotten. We speak of the phlegmatic person without meaning that he suffers from any affection of the upper respiratory passages; the sanguine is not particularly bloody-minded; and the bile of the melancholic is the same colour as ours, though the bilious influence survives today in the tube-train advertisement of a liver pill. This may remind us how psychological medicine is rich in words that don't mean what they say: lunacy, hysteria, and hypochondria no longer call up ideas about the moon, the womb, or something under the ribs. Neurasthenia was losing the connotation of an asthenic neuron when it almost passed out of use—unfortunately, I think, for words that plainly don't mean what they say have advantages. The gynæcologist, for example, takes no interest in the soldier with hysteria.

In later ages Galen's temperaments fell out of fashion, and every advance in science was seized upon as giving the final explanation of what makes the wheels go round. Sometimes the new force was hailed as superseding animism; sometimes it was an expression of it. Vigorous controversy often took place, the significance of which is hard to understand without knowledge of its relation to problems of the period. Van Helmont (born 1577) made play with the archæus of Paracelsus and its relations with fermentation. Sylvius followed with vital spirits that were prepared in the brain by distillation, and Harvey's discovery of the circulation of the blood served Stahl to give a mechanistic support to his animism and explain that "the mind adopts and maintains as its fundamental disposition that particular disposition which the movement of the humours through channels of a definite type has given to the pulse or circulation."

STAHL'S PSYCHOLOGY

Stahl was in my student days held up as a bogy man. His theory of phlogiston, an explanation of combustion, was so absurd that the use of a pair of scales would have disproved it, yet in some curious fashion it was said to have hindered the progress of chemistry for a hundred years. His theory of animism was presented as a cantankerous belief that bodily processes did not follow the laws of chemistry or physics, and was finally disproved by the synthesis of urea.

When Greenwood and Smith (1934) went to original sources they found a different story. Stahl was an efficient chemist and anatomist; his theory of phlogiston was not absurd for his period; phlogiston was no more a material substance than was heat or cold, and no reasonable man would expect to weigh it. He claimed, however, that chemistry and physics were given more than they could carry and propounded a psychology which, to the disadvantage of medicine, fell as seed upon stony ground. His description of psychological types will bear comparison with that of Jung and he shows how a sound mechanistic training combined with the scientific spirit—which I define for this argument as the unprejudiced search for truth—will drive the clinician to the use of psychological conceptions.

Greenwood and Smith note that there were scientific giants in those days, and that Stahl lived in an age that was reaping the effect of the work of Copernicus, Galileo, Kepler, Harvey, and Descartes. We know that opposition was active; the battle of theology versus science was raging and influenced a trend on one side towards making chemistry and physics all-sufficing. After a vigorous controversy, chiefly with Leibnitz, Stahl was defeated, and his defeat set back the progress of psychology in medicine for two hundred years.

HALLER'S IRRITABILITY OF NERVE

After Stahl came von Haller. A good physiologist, by close and accurate work he established the irritability of nerve and all unsuspecting, laid the foundation for great material advance and great immaterial speculation. This irritability was soon turned into a nervous force, and again the final solution had been found. Sprengel (1803) declared "all the phenomena of life, especially the movements of the solids and the mixture of the humours, are the results of the influence of the nervous force." In 1925 Seelig wrote:

> These studies substituted for the Hippocratic principle of the pneuma, for the archæus of Paracelsus, for the vital spirits of Sylvius and for the anima of Stahl, for all these vague meaningless things these studies of Haller substituted the simple principle of irritability, a force now recognised and experimentally demonstrable in all living tissue.

The background to this enthusiasm is to be found in the fact that Seelig, writing an up-to-date history of medicine, makes no mention of psychology, offering not even a refutation of Freud. The irritability of nerve had put such nonsense permanently out of court.

Von Haller (1747) had no share in such claims. He would, I think, have repudiated them, for he wrote after mentioning some current theories: "We shall refer them to those hypotheses which the desire of explaining those things of which we are unwillingly ignorant has given rise to." He indicates here a pitfall into which medicine has repeatedly fallen.

THEORY OF EVOLUTION

The 19th century saw an old situation repeated when the evolution theory set off again the ancient battle. Huxley, Darwin, Romanes, and Herbert Spencer were among the intellectual giants of that age and they put up a lively fight; a notable skirmish in the campaign being that between Huxley and Gladstone about the

* Valedictory presidential address to the British Psychological Society at Exeter, April 7, 1945.

[1] Some years ago I asked the late William McDougall why the American favoured Watson's behaviorism. He answered that it was a political matter with some connexion with the possibility of making 100% American out of East European immigrants. It is possible that Pavlov's privileged position in revolutionary Russia depended on a recognition that his theory of conditioned reflexes gave hopes of altering the reactions of the rising generation in a desired direction. Many years before this, Benjamin Kidd in his *Science of Power* had shown the possibility of altering in one generation the collection of emotional and behaviour patterns that he called "social heredity." But he found no heed to heeded about conditioned reflexes.

Gadarene swine. Again the ranks had to be closed, and a bugle-call is sounded in the OED definition of *neurosis* as "a change in the nerve-cells of the brain prior to, and resulting in, psychic activity" This definition, supported by references to Huxley and Romanes, is not physiological but metaphysical, and anyone who feels like it is free to reverse the process and make the psychic activity precede the neuronic. You can't check it under the microscope

To admit the possibility of the psychosis preceding the neurosis might have been equivalent to a surrender that by some process of argument would ultimately lead to a belief in the historical accuracy of the story of the swine. Whatever the forces at work, there was an urge to deny validity to psychological conceptions This came to apotheosis in Pavlov's work on the conditioned reflex, at the mention of which the medical psychologist is expected to bow his head and worship silently at the shrine of pure science.

PAVLOV'S CONDITIONED REFLEXES

This work goes back to the 19th century and belongs to it As a student I thought that Pavlov, working in a spirit of pure research, had discovered this reflex and then found it of wide occurrence in physiological mechanisms But a film picturing his work, and shown some years ago at the Royal Society of Medicine, finished with the statement "Man's behaviour is but a series of *conditioned reflexes*" Surely, thought I, Pavlov never said that, he's a scientific man So I turned to the original and found that he *did* say it His account tells how he set out to find a scheme of animal and human behaviour that would exclude psychological conceptions, and he produced it by this elaboration of his conditioned reflex

Here we see a new departure Instead of taking the latest discovery of science and claiming for it, in time-honoured fashion, the final solution of the basic problem of metaphysics, Pavlov looked around for a new scheme by which he might propitiate the mechanistic gods This negation of the spirit of research was not easy Or was it too easy? Listen to this and judge for yourselves:

> "The dog" (previously described as very tractable) "was placed in a stand with loose loops round his legs, but so as to be quite comfortable and free to move a pace or two. Nothing more was done except to present the animal repeatedly with food, at intervals of some minutes It stood quietly enough at first, and ate quite readily, but as time went on it became excited and struggled to get out of the stand, scratching at the floor, gnawing at the supports, and so on This ceaseless muscular exertion was accompanied by breathlessness and continuous salivation, which persisted at every experiment for several weeks, the animal getting worse and worse until it was no longer fitted for our researches For a long time we remained puzzled over the unusual behaviour of the animal. We tried out experimentally numerous possible interpretations, but though we had had long experience with a great number of dogs in our laboratories, we could not work out a satisfactory solution of his strange behaviour, until it occurred to us at last that it might be the expression of a special *freedom reflex* and that the dog simply could not remain quiet when it was constrained in the stand." Pavlov (1927)

He describes his investigation of a case of catalepsy and tells us that "Owing to many previous years of experience in the laboratory I reasoned on a purely physiological basis" When he gets down to the pathology he offers us the choice of "toxic action," "an exhaustion of the elements of the cortex," or "direct or indirect reflex influences (the last resulting from local changes in the blood circulation or in the general nutrition)" The words belong to physiology, but the ideas are fantasy and, taking a lead from the great man himself, I propose to invent and invoke a *fantasy reflex* When this is suitably conditioned, the presentation of a psychological problem produces an outpouring of fantasy which is expressed in physiological language and, if from one in authority, comes to be accepted as scientific truth Here is an example of this reflex from a standard textbook used by students in the darkest period of medical psychology—i e, about 1900 It is an explanation of writers' cramp

> "The education of centres which may be widely separated from each other for the performance of any delicate movement is mainly accomplished by lessening the lines of resistance between them, so that the movement, which was at first produced by a considerable mental effort, is at last performed almost unconsciously If, therefore, through prolonged excitation, this lessened resistance is carried too far, there is an increase and discharge of nerve energy, which gives rise to spasm and disordered movement"

Orations and essays on medical education dwell upon the need for teaching the student to think for himself. For such an end this passage could provide an excellent lesson, but at the cost of arousing disrespect for authority Without this disrespect the student must feel that the author has access to wells of truth hidden from ordinary folk, or possesses an esoteric faculty of diagnosis which he, poor fish, can neither emulate nor question.

MAUDSLEY'S NEUROSIS SPASMODICA

Returning to the days of Victorian controversy, we find another example. Maudsley, a famous psychiatrist and a contemporary of Romanes and Huxley, could not escape the metaphysics of his day He took over the neurosis idea, gave the word a new pathological meaning (it already had several old ones), and invented a *neurosis spasmodica* which underlay (or perhaps was prior to and resulted in) the insane temperament. He defined it as "a defective or unstable condition of nerve element, which is characterised by the disposition to sudden, singular, and impulsive caprices of thought, feeling, and conduct" Maudsley (1879) has walked into the pitfall indicated by Haller and produced a fantasy the only function of which is to allow us to think we know something when we know nothing It is strange that today "neurosis" does not indicate the physiological basis of insanity but any mental disorder that is not insanity. I cannot trace when or how this change came about. In 1870 Maudsley wrote (the quotation is to be found at the front of a recent textbook on *Physical Methods of Treatment in Psychiatry*)

> "The observation and classification of mental disorders have been so exclusively psychological that we have not sincerely realised the fact that they illustrate the same pathological principles as other diseases, are produced in the same way, and must be investigated in the same spirit of positive research Until this is done, I see no hope of improvement in our knowledge of them, and no use in multiplying books about them"

CHARCOT

The establishment of this dogma that mental disorders illustrate the same pathological principles as other diseases was accompanied by two extraordinary episodes

Charcot was a neurologist whose name filled me as a student, with awe In the late 'seventies he set out to examine hysterical phenomena by the same methods he found so useful in the investigation of nervous disease. He studied changes in the state of muscles, in reflex movements, and the degree of various sorts of sensitivity, and the results are scarcely to be believed You may remember Axel Munthe's story of the kitchenmaid he tried to rescue from Charcot's clinic Munthe could tell a good story, but the clinical side of this one accords exactly with Charcot's own accounts of how he discovered symptoms in his patients—or, rather, how he produced those symptoms and then accepted them as real THE LANCET of 1882 contains vigorous articles from a Paris correspondent identifying Charcot's methods with those of the animal magnetists of a century earlier. Finally, Bernheim demonstrated that the elaborate syndromes described by Charcot were the result of his own unwitting suggestions to the patients, and the whole affair was buried with as little fuss as possible instead of being recorded as an instructive mistake.

In 1920, after publishing a book on the war psychoneuroses, I received a letter from Herbert Page, a surgeon who was then just a name to me. He had read my book and wanted to tell me that all the symptoms of shell-shock were described in his book on *Railway Injuries* (Page 1891), but that the lesson he had tried to teach had been forgotten This sent me to Erichsen's (1877) account of railway spine, a condition resulting

from railway accidents and in my student days still mentioned in the textbooks but attributed to "traumatic neurasthenia." Erichsen was the leading surgeon of his day, but his mechanistic blinkers led him into a mistake as great as Charcot's. He described at length symptoms that I have seen only in a wardful of untreated and titubating shell-shockers, for these he invented a pathology of myelitis, meningitis, ascending and descending spinal degeneration, and whatnot, while his patients were pushed downhill just as Charcot's were. It took Herbert Page years to destroy this mythopathology and, like Charcot's mistake, it was again buried as quietly as possible. I met Herbert Page later on and in talk with him happened to use the word "psychology." He shook his head. "I don't know anything about psychology," said he, "I only know it was something the matter with the man himself!" His mechanistic training, together with the scientific spirit, had driven him, like Stahl, willy nilly into the use of a psychological conception.

Charcot's fantasies were for years accepted by his colleagues in France, as were Erichsen's in this country. Charcot and Erichsen were experienced men of high intelligence, but intelligence and experience were, and still are, no protection against the results of a fundamentally false assumption.

SHELL-SHOCK AND NIGHT BLINDNESS

Then came the war to end war, and high explosives introduced a new disorder, shell-shock. How many of you know that casualty reports used to contain the heading "wounded; shell-shock"? Again fantasies were produced, this time about separated synapses, dissociated cerebral centres, punctiform hæmorrhages (which really did occur in other conditions), and so on. In 1916, at a hospital in France, I found myself in a minority of one when I maintained that shell-shock was a mental phenomenon not produced by the physical effect of high explosives on the central nervous system. Still, *magna est veritas*, and before the end of the war the use of the phrase "shell-shock" was prohibited, and the authorities set up training-centres to teach medical men psychology so that they could treat these cases. Herbert Page was right; the lesson of railway spine had been forgotten.

You may be thinking such things don't happen now. But they do, and you have lately seen the rise and fall of another fantasy. You remember about three years ago there appeared, in staid and respectable journals like *Punch* and the *Times*, pictorial advertisements showing what the nocturnal streets looked like to the night-blind, and what they looked like to people made healthy by something or other out of a bottle. These advertisements suddenly ceased, and behind their appearance and disappearance is a long story.

Night-blindness has occurred as an epidemic in armies since the time of the crusades, and in the earlier war it was so prevalent in the continental armies that over 45 communications about it appeared in French, Belgian, and German periodicals, giving, I would guess, almost that number of hypotheses about its cause, for it was thoroughly investigated from every aspect except the psychological—the only one that mattered. I saw no case in 4½ years service and can find only one reference in our literature. Lieut-Colonel (now Sir Herbert) Eason (1917) noted 23 cases in Egypt, but recognised the nature of the disorder and did not popularise it.

Just before the start of this latest war the idea arose that loss of dark-adaptation (the failure of which is equivalent to night blindness) could be used as a measure of vitamin deficiency, and some people thought they had proved it. Perhaps they had, perhaps they hadn't; it is risky for people with no psychological outlook to investigate a subject so full of psychological pitfalls. Interest in it grew, however, and much was made of it. My recollections led me to see danger, and I wrote to a medical journal (Culpin 1940), giving the history of night blindness in the last war and suggesting that we had escaped the epidemic then because we didn't happen to think of it. But, I added, if we talk enough about vitamins and night blindness we may start an epidemic; then psychopathologists will declare the nature of the disorder and will be derided at first; but, when the epidemic is well established and the cases are thoroughly ripened, they will be called upon to treat it.

It all came true. The epidemic arrived and one quasi-scientific paper appeared in *The Lancet* in 1941 reporting a study of night blindness in soldiers[2] due to vitamin deficiency. It was full of graphs and tables and correlations that didn't correlate the right way up—a beautiful example of the fantasy reflex. Everyone by now had heard about night-blindness. Radio comedians put it in their gags, the advertising quacks cashed in on it and vitamin fans ate carrots till their skins turned yellow. But Wittkower et al. (1941) at Glasgow studied some sixty cases, demonstrated that the symptom was psychogenic, and published their paper in the same journal that had printed my warning. In due course a neurological colleague took his share in the fulfilment of prophecy and was delightfully derisive of their work (Walshe 1941). Finally a confidential memorandum was sent to Army ophthalmologists telling them that for practical purposes night blindness did not exist in the absence of gross ocular disease, and any difficult cases should be referred to the psychiatrist.

These secret burials must be discouraged; they waste valuable museum specimens.

PSYCHO-ANALYSIS

Now let us go back and note developments. Long after the turn of the century the student heard nothing about psychology. "Functional nervous disorders" occurred, but there was no idea of positive diagnosis such as we make today; recognition rested upon the absence of organic disease, and the diagnosis was rare, since the conditioned reflex was always at work and some disease or other could always be imagined; but if a chief was omniscient enough to diagnose by exclusion a functional nervous disorder, the patient was hustled off the premises as speedily as possible, though paradoxically this was the period of pexies, when kidneys, colons, stomachs, and wombs were trussed up by ingenious surgeons, partly in the belief that ptosis of organs was a cause of neurasthenia.

Yet a ferment was at work. McDougall (1915) raised something of a storm by basing human conduct on primary instincts. Freud and Breuer (1893) published accounts of treatment by reviving memories, and the gradual unfolding of psycho-analytical theory and practice followed, while Janet set out his useful theory of dissociation of consciousness. This dynamic psychology had something to offer to medicine, and war needs brought about its application. It was a direct challenge to the principle defined by Maudsley some forty years earlier, and the war cases focused the heat of one of the most bitter attacks ever made on new ideas.

Psycho-analysis took the brunt of the attack, but the fundamental struggle was between a dynamic psychology and the exclusive mechanistic conception. I recall my bewilderment at the opposition to what, in my ignorance, I had regarded as an unobjectionable though novel approach to the war cases—the revival of war memories and working off of the associated emotion. Sometimes this was labelled psycho-analysis, and discussion would be drowned in a flood of sexual expostulation; or it would be denied that memories had been lost or that if lost they could be revived—claims to revive them being met with the charge that the operator suggested imaginary episodes to the patient or, per contra, that the patient, artful neurotic, made up stories to fool him. That last was the view of Sir William Osler, who after I had once been rash enough to describe revival and abreaction arose in his genial way and, thumbs in armholes, declared "I'm a bit of a liar myself. I could make up stories and imitate emotion in a way that would deceive my young friend over there." Realising that I had in all innocence challenged the foundations of belief of the greatest physician of his day, I can look back on this incident with purely historical interest.

A result of the opposition was that the method found no place in psychiatric textbooks and in the next war was greeted by some of the younger generation as a new discovery. Curiously, much of the opposition came from psychiatrists. The innovators, many of whom passed from the war work of 1914–18 into civilian

[2] I assume it was in soldiers. If it was in civilians it [illegible] war more severe than I thought.

psychological practice, called themselves psychotherapists and were concerned by choice with the minor psychoses or psychoneuroses rather than with the major psychoses or insanities, though the true distinction was between the two opposing basic assumptions This affected the British Psychological Society, for the modern school needed a spiritual home and found it in our medical section, the membership of which showed hardly any overlap with that of the Royal Medico-Psychological Association, then chiefly concerned with the mental-hospital side

TREATMENT AND INSTRUCTION

For a long time the teaching hospitals took little interest in the new developments, and the London Hospital Medical College seems to have been years ahead in setting up a lectureship on the psychoneuroses in 1919 To meet an obvious need independent clinics were established where both treatment of patients and instruction in the subject were provided These clinics received little or no official support and had to appeal to the charitable public.

Great things were expected from the Maudsley Hospital, opened about 1920, it has done excellent work within its own sphere, and to have been trained at the Maudsley is a hallmark for the English psychiatrist, but the teaching there has followed, with its advantages and disadvantages, the principle enunciated by Maudsley and quoted earlier in this paper, and it was common for men trained there who wished to learn something of the other mode of approach to seek it at one of the clinics

Gradually the new ideas have penetrated into medicine generally and into psychiatry, which has largely absorbed not only the principles of psychotherapy but also its practitioners. The rising generation of psychiatrists, if left to themselves, seem capable of abolishing what may be the false antithesis that has plagued us through the ages, and of unifying the two points of view—the study of physiological mechanisms and the study of the reactions of the man as a whole—while admitting that somewhere is a gap in human knowledge which we must not pretend to bridge but recognise as a fit subject for metaphysical speculation by those who find pleasure in such exercise. This prospect makes one regret that the Goodenough report on medical education (Ministry of Health 1944), while giving full consideration to the needs of education in psychiatry and offering excellent advice about it, has made recommendations that would perpetuate a one-sided teaching

After asking why the provision for training in psychiatry failed to keep pace with the growing realisation of the important place the subject should occupy in medical thought and practice, the report suggests three reasons that can be summed up in the simple statement that the teaching hospitals would have none of it A fourth reason is a strange display of acrobatics · here it is

> "Owing to the limited opportunities for work in the teaching hospitals, most of those psychiatrists who did not wish to confine their interest to the psychoses and to work in mental hospitals have been compelled to give their services to clinics separate from, and independent of, the medical schools and teaching hospitals Many of these clinics have met a real need and have provided useful courses of training, but their detachment from the main body of medical education and practice has deprived their staffs of that contact with other branches of Medicine which is necessary for progress and the preservation of a true perspective, and has weakened their influence on the development of medical education"

Where *was* this true perspective? Was it among the staffs of the hospitals that for years refused to touch the subject or was it among the staffs of those pioneer clinics that educated our profession and the public till the teaching hospitals were compelled to accept their responsibilities? On the same page that registers these acrobatics the report specifies that psychiatrists who teach students must be "of broad views and balanced judgment" Later on we read that "The essential lesson about the relation between physical and mental data can be taught effectively in a department in which neurology and psychiatry are linked, . ." What metaphysical speculation lurks in this essential lesson is not clear, but no doubt must be cast upon it, for lower down we are told "The important thing is to select someone who will give good teaching on normal psychology, on lines that are broadly conceived, that avoid sectarian disputes, and will eventually serve medical ends" In no other clinical or preclinical subject would the writers of the report have dared thus to lay down specifications for an academic yes-man All is to be ready for turning out the student like a pithed frog, with his Pavlovian reflex tuned up to produce more fantasies in the approved pattern The clinics, already praised with faint damns, are now to be sunk The report indicates unwittingly but clearly that the Maudsley Hospital, backed by the resources of the London County Council, did not satisfy a real need which the clinics met for twenty years or more This failure arose from the fundamental assumptions of the Maudsley tradition, yet the report is enthusiastic about the hospital and looks forward to the development of the teaching of psychiatry aided by "the vast resources and wealth of facilities" of the LCC mental-health services till they become "the European centre of progress in psychological medicine." A broad view indeed, but terrifying!

LINES OF ADVANCE

In spite of the one serious defect the report stands out as a comprehensive statement of the present situation and its needs Other important bodies are giving earnest consideration to these needs, and it is plain that great changes are taking place that will surely be of historical importance It is significant that Sigmund Freud became a fellow of the Royal Society and an honorary fellow of the Royal Society of Medicine There now appear as a matter of course in our journals articles of psychological moment that would have been greeted with derision a few years ago if anyone had been brave enough to write them Those who went through the mill in the last war (they were called neurological specialists in those days) can best appreciate the wonderful advances in Army psychiatry of today, which calls for more attention than can be given here Members of the British Psychological Society have had their share in the pioneer work that has helped to bring about these changes, but I foresee that our medical section will develop along new lines, for the clinical psychologist, whatever his point of view, can now be at home in the Royal Medico-Psychological Association

There is, however, a growing knowledge of the social implications—cultural, industrial, or educational—of personality difficulties and the minor, if not the major, psychoses Our medical section will remain as the liaison between medical psychology and these applications, in wider spheres, of knowledge derived from the study of the individual

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"'A room of one's own' for the children is the ideal to aim at, so as to give them freedom in the home and not only outside it But you cannot get that unless you have warmth and comfort, not merely in a single living room or kitchen, but in every room We are incredibly behind other countries in warming our homes, and the result is that we do not make proper use of the space we do provide"

Prof J. M MACKINTOSH, *Listener*, Oct 4, p 374

TRAUMATIC HÆMOTHORAX AND HÆMOPNEUMOTHORAX

DIAGNOSIS AND TREATMENT

T SIMPSON

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LIEUT -COLONEL RAMC FORMERLY SPECIALIST PHYSICIAN TO NO 3 CHEST TRAM IN BLA

In the repeated examination and aspiration of some 700 recent war wounds of the chest, the following points of practical value emerged concerning physical examination and aspiration of the chest

PHYSICAL EXAMINATION

In the doubtful lesion, where diagnosis was not obvious, it was evident that there were several factors hindering diagnosis Thus, both penetrating and non penetrating wounds of the chest could cause immobility of the injured side and so give rise to confusion in the interpretation of physical signs. Secondly, surgical emphysema of the chest wall produced such gross alterations in percussion and auscultation that its presence had always to be sought If it was extensive, then diagnosis by physical examination alone was impossible Thirdly, I found that the positions of the trachea and apex beat were of no real value in the elucidation of the doubtful case These limitations must be borne in mind in the discussion of the diagnosis of hæmothorax, pneumothorax collapse, and consolidation occurring either singly or in combination Points in the differential diagnosis are stated in order of importance

Hæmothorax —(1) Stony dullness on percussion and absence of tactile vocal fremitus are the two most important physical signs

(2) Breath-sounds may be present even with a large hæmothorax Indeed, they are more often distant bronchial in character, indicating the collapsed state of the underlying lung The vocal resonance is correspondingly altered

(3) It is impossible on physical and radiological examination alone to estimate the amount of blood in the pleural cavity

(4) Massive clotting was suspected when the physical signs suggested a large hæmothorax, except that there was no displacement of the trachea or apex beat, and aspiration had failed

The *differential diagnosis* of hæmothorax is from basal collapse of moderate severity and from basal consolidation In such *basal collapse* the following points are important

The clear-cut limitation of the physical signs to the paravertebral region in basal collapse proved to be of the greatest help if the limits extend to the axilla hæmothorax is almost a certainty

The character of the bronchial breathing in basal collapse more closely resembles that heard in consolidation

Moist sounds are heard in the lung more often with basal collapse than with hæmothorax

The dullness is never so absolute as in hæmothorax

In the differential diagnosis of hæmothorax from *basal consolidation* the following points are important

The tubular quality of the breath-sounds usually distinguishes basal consolidation from both hæmothorax and collapse

Numerous moist sounds especially post tussive, are heard in the affected lung

Tactile vocal fremitus is always present and usually increased in intensity this is never so in either hæmothorax or collapse

The limits of the altered physical signs are not so clear-cut in basal consolidation as in collapse but they are of little help in the differentiation from hæmothorax

Confusion existed in most minds between the diagnosis of collapse and consolidation the latter being diagnosed more frequently The history must be taken into account in establishing the diagnosis For instance, collapse might be expected after an abdominal injury or operation, or where the patient had coughed up much blood, or where the altered physical signs were found in the contralateral lung after a chest wound Furthermore, the temperature was often more elevated in consolidation, and collapse, though sometimes insidious in onset was usually accompanied by dyspnœa out of all proportion to the extent of the physical signs or the general condition Diagnosis was not usually difficult and fortunately so, for the implications of a missed collapse can readily be appreciated

Pneumothorax —(1) A hyperresonant percussion note in the absence of surgical emphysema of the chest wall and even in the presence of diminished breath sounds, is pathognomonic of a pneumothorax.

(2) Well marked diminution in the intensity of the breath-sounds may be produced by fixity of the chest wall (see above), but their character remains vesicular and the percussion note is unaltered

(3) In the diagnosis of a shallow pneumothorax it is important to remember that the altered physical signs may be present not anteriorly but only posteriorly at the apex

(4) On physical examination alone a fair estimate can be made of the size of the pneumothorax

ASPIRATION

My aim in aspiration was to secure complete expansion of the lung at the earliest possible moment This was effected in most of the cases treated within a few hours of wounding Later it was more difficult Where operation was necessary, as in closure of a sucking wound aspiration was done in the theatre, and, in the absence of gross damage to lung complete pulmonary expansion was invariably obtained (Subsequent aspirations never numbered more than two) I was left with the impression that most of the complications of hæmothorax and pneumothorax could have been avoided if the chest had been aspirated early and assiduously

At each aspiration I removed as much air or blood as possible without causing too much distress to the patient, and my opinion has been that when air and blood are present in the pleural cavity it is more important to remove the air This will be discussed more fully under hæmopneumothorax

Hæmothorax —A modified Potain set with a Maxwell induction needle and a Winchester quart bottle as receptacle, was the standard apparatus used, with the addition of a syringe and a detachable two way tap for difficult aspirations

Although most chests were aspirated in the 9th space posteriorly, it cannot be overemphasised that each case was approached individually and the exact site determined for the particular condition A common finding was that a collection of clot posteriorly made aspiration easier from the axilla, and in cases requiring several tappings it was usually necessary to insert the needle a little higher and more laterally as the aspirations proceeded During axillary aspiration, if the flow of blood increased with inspiration and decreased with expiration, one could be sure that the chest was almost dry, the more so if shoulder pain was produced If aspiration was difficult or unsuccessful, the patient was radiographed in the postero anterior and lateral positions and the case reviewed since blind aspiration is most dangerous

The intervals between aspirations varied, depending on the amount of air or blood removed My practice was to aspirate on at least alternate days

The character of the aspirated blood often gave valuable information If it was bright red and did not clot on standing I felt reasonably certain that I could drain the pleural cavity completely If the blood clotted on standing was dark and thick and difficult to obtain or was more fluid but contained soot like particles, I always suspected clotting in the hæmothorax Early infected blood was like red ink, and late infected blood was brown and often malodorous

Finally, I found that the clearance of pockets of fluid by aspiration alone was impossible

While the aspiration of the uncomplicated hæmothorax in the light of the physical and radiological examination presented little difficulty, new problems arose in the treatment of a hæmopneumothorax

Hæmopneumothorax —A completely collapsed lung will inevitably lead to a total pyothorax if infection of the pleural cavity supervenes Further, as the apex of the lung is the most difficult part to expand in the later stages of treatment it has been my practice to remove at the earliest possible moment all the air from cases of

hæmopneumothorax, to secure adhesion between the apex of the lung and the parietal pleura Then, if infection does supervene, one has at worst a localised empyema.

The only satisfactory method for removing all the air from the pleural space is by apical aspiration, done by inserting the needle at a point midway between the vertebra prominens and the medial angle of the scapula with the arm at the side. By passing the needle downwards with a slight inclination forwards, the pleural cavity is entered very close to the apex All the air and a surprising amount of fluid can be removed The air at the apex was replaced by a cap of fluid from which no deleterious effect was observed Where the amount of blood in the pleural cavity was large, apical aspiration was immediately followed by basal aspiration

Complete pneumothorax—Aspiration was first done through an anterior approach in the 2nd interspace with the patient in the semirecumbent posture. Clearly all the air could not be removed, as the expanding lung blocked the needle at a subapical level Pressures were taken initially and at the end of the aspiration of about 300 c cm of air If the final pressure was the same as the initial one, or if being a higher negative it was not maintained, the presence of a bronchial fistula could be presumed. When this was so, aspiration was repeated once or twice daily in the hope that the fistula would close If this did not happen within two days, surgical measures had to be undertaken In the absence of a bronchial fistula apical aspiration was adopted as for hæmopneumothorax

SUMMARY

From experience gained in repeated examinations and aspirations of the chest in some 700 war wounds of the thorax, points in the diagnosis and the value of aspiration are emphasised, with particular reference to hæmothorax, pneumothorax, hæmopneumothorax, collapse, and consolidation

Aspiration should be begun early to secure complete expansion of the lung as soon as possible and to prevent complications of hæmothorax and pneumothorax

Different methods of aspiration for hæmothorax, hæmopneumothorax (apical aspiration), and complete pneumothorax are described

My thanks are due to Major J L Collis, RAMC, surgical specialist to the team, for his advice and suggestions

DIRECT IRRADIATION OF CANCER OF THE STOMACH AND OTHER VISCERA

EXPOSED TEMPORARILY AT OPERATION

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GASTRIC cancer is the commonest form of cancer and gives the worst results from treatment Only 1–4% of 5-year cures follow curative surgery, and only about 4 months' longer life is gained by palliative treatment (Livingston and Pack 1941, Schindler 1941). Some of the reasons are as follows

(1) Too late diagnosis, some 80% of cases of gastric cancer are beyond any hope of cure by surgery when first brought to the surgeon (Ogilvie 1938)

(2) Incomplete surgery, even in early cases, the disease not being completely extirpated

(3) The failure of irradiation, which has been tried in various forms and combinations but without striking success By many it is thought not only to shorten the patient's life but also to add to his suffering and therefore to be unjustifiable While this may be true of other methods, direct irradiation at high intensity has none of these disadvantages, while treating the lesion and field of local spread with minimal damage to adjacent tissues and viscera

External irradiation fails because of the deep situation of the gastric tumour and its close relation to other vital organs, both factors tending to prevent adequate tumour dosage, and because of the high but variable radio-resistance of gastric cancer-cells, possibly increased by infection This high resistance may be only apparent, owing to limitation of the tumour dose by general and skin reactions Accurate centring of the X-ray beam at repeated exposures is difficult, owing to movements of the tumour

Contact therapy with the Chaoul tube covers such a relatively small area (2 cm diam) in each field, with very little penetration at low voltage Pack (1939) found that only 22% of the surface dose penetrated to 1 cm. below the surface. Bulky tumours could not be destroyed by single surface doses at one operation but needed repeated exposures With such a small field repeated applications would be required for most inoperable tumours, with the obvious difficulty of adequate and uniform dosage. Such localised irradiation would have no appreciable effect on any glandular or other local spread, the presence of which is the usual reason for inoperability

Radon seed implantation has the same difficulties of uniform and adequate dosage, as shown by subsequent radiography There are also dangers of hæmorrhage and infection, and perhaps perforation due to massive necrosis of the while the adjacent field of spread does not receive [illegible] irradiation

Intracavitary irradiation with the 5-way tube used by Livingston and Pack (1941) has, they claim, the advantages of easy application, fractionation of doses, avoidance damage to adjacent vital organs, freedom from dangers of perforation, hæmorrhage, and infection, and no [illegible] with food intake. But they had not yet (1941) [illegible] how effective a total dose patients would stand, the effective fractions into which to divide the total dose, or the results as regards palliation or cure Used alone it would appear to have much effect on local spread, but combined with direct irradiation it might well be used to supplement the dose reaching the centre of large gastric tumours

DIRECT IRRADIATION

Because of these failures in the attack on gastric cancer, we put forward a scheme of combined surgery and direct irradiation for surgically inoperable cancer The results of external irradiation at high intensity in many hopeless cases of malignant disease had been encouraging, but in view of its limitations (see above), Fairchild (1935) began to work out a scheme for direct irradiation of deep-seated tumours Some cases of rectal cancer were treated by external irradiation applied posteriorly after turning back skin-flaps over the sacrum and coccyx By this means adequate dosage was not obtained; so fractional doses were applied daily for a week or 10 days But the wound became infected when kept open for so long, and the method was abandoned. Further progress was held up until Fairchild and Shorter (1944) began to work out a technique for the direct irradiation of gastric cancers exposed temporarily at operation, as had been originally intended, instead of merely turning back skin-flaps The method was later elaborated to deal with cancers of other viscera

ADVANTAGES OF THE METHOD

More accurate information about the size, shape, position, and extent of the primary lesion and any local or general spread (abdominal or thoracic) can be obtained at the exploratory operation than can be found out by any other methods, clinical or laboratory. Exploratory operation is the only reliable way of deciding the correct form of treatment (Walters et al. 1942) Treatment had to be abandoned in many patients owing to unsuspected widespread metastases

Biopsy specimens can usually be obtained to help confirm the diagnosis With glandular spread this can be done safely, but incision of the tumour may lead to perforation owing to the subsequent massive irradiation

A more accurate and effective dose of irradiation at high intensity can be given directly to the tumour and field of local spread, without irradiating such a large volume of normal tissue, including vital organs and skin, unavoidable when irradiating from the skin surface This may be of vital importance in an already anæmic and cachectic patient

More accurate centring of the X-ray beam is possible under direct vision than when relying on X-ray films or clinical examination alone

The skin is left practically intact and will permit further full dosage to be given externally at a later date if necessary. External irradiation was given later in some of our earlier cases, because we thought that the initial dose was too small to cure

Various operations to relieve obstruction can be done before the irradiation—e.g., gastrostomy for lower œsophageal or cardiac tumours, and gastrojejunostomy for pyloric lesions. Though the obstruction may not be severe, it increases owing to fibrosis of the tumour following irradiation. In hopeless cases these operations can be done without irradiation to relieve symptoms.

PRELIMINARY INVESTIGATIONS AND PREOPERATIVE PREPARATION

Diagnosis and localisation of the tumour are achieved as accurately as possible by clinical, radiological, gastroscopic, œsophagoscopic, and *laboratory investigations*. The general condition of the patient is investigated as regards possibility of metastases, state of nutrition, and suitability for operation and anæsthesia.

Patients with cancer of the upper alimentary tract are often bad risks for operation. This varies considerably with the site and type of growth, the degree of interference with nutrition, infection of the tumour, and toxæmia from the growth. The patient with cancer of the œsophagus, cardia, or pylorus is a worse risk than the patient with a mid-gastric lesion, owing to the more profound disturbance of nutrition, even amounting to *gross deficiencies of many vitally important substances*.

These deficiencies must be made good before any extensive operation is carried out (Wangensteen 1943, Payne 1940, Garlock 1942, Ravdin et al 1943, Reid 1941). This includes restoration as far as possible to the normal level of hæmoglobin and blood-cells, blood plasma proteins, salts, vitamins (A, B and C especially), body fluids, and liver glycogen (replacing fatty deposits). The necessary food substances are given by mouth, gastrostomy, or jejunostomy in the form of a high-protein, high-carbohydrate, low fat diet, with extra fluid, iron, salts, and vitamins when necessary. Beef juice and liver juice are valuable in restoring plasma proteins, as are blood plasma infusions. Blood transfusion may be necessary, and in urgent cases amino-acids, vitamins, iron, &c., are given by injection.

Infection is combated in the tumour, or in the stomach generally in pyloric obstruction, by daily gastric aspiration and lavage with weak HCl solution. Dental sepsis, so often associated with upper tract cancers, is attended to, especially before general anæsthesia. A prophylactic course of sulphathiazole is begun 2–3 days before operation to minimise the risk of postoperative sepsis, abdominal or pulmonary, and continued as soon as possible after operation. Routine breathing and coughing exercises (Shorter 1944) are begun before operation and continued as soon as possible after operation, to maintain a clear airway and good expansion of the lungs. This is most important in all upper abdominal operations, especially when the thorax is opened also.

SURGICAL APPROACHES

(1) *For Lower Œsophageal and Gastric Cancers*.—This may be in one or two stages. When there is well-marked œsophageal, cardiac, or pyloric obstruction, gastrostomy, or jejunostomy may be necessary before the patient's condition can be improved sufficiently to stand the wider exposure and irradiation. This is usually done through a small upper left paramedian incision, through which exploration of the abdomen is possible, giving information about the growth and its spread. Many cases have in this way been found unsuitable for irradiation. When the patient's condition is satisfactory, the tumour is exposed by a much wider incision.

(a) *Midline Incision*.—In our early cases the main approach was through a midline incision from umbilicus to sternum, excising the xiphoid process. With a narrow subcostal angle, the wound was widened by dividing each costal margin and forcibly retracting. Then the tumour was mobilised to bring it down into the open wound. This method was abandoned later in favour of leaving the tumour in situ and retracting the abdominal and perhaps thoracic wall to give direct and wider exposure.

(b) *Angular Abdominothoracic Incision*.—For upper gastric and lower œsophageal tumours a transverse incision was made through the 6th and 7th left costal cartilages from the upper end of the midline incision, and continued round in the 5th space to the posterior axillary line (fig. 1a). The thorax is opened and the left side of the diaphragm is divided down to the œsophageal hiatus, the incision skirting round the left edge of the pericardium. This method caused less operative shock and decreased the risk of spreading the disease by lymphatic embolism owing to decreased manipulation of the tumour. Also it gave better direct access to the cardiac region, though some difficulty was experienced in retracting the angular flap containing the divided left costal margin.

(c) *Oblique Abdominothoracic Incision*.—In our later cases this difficulty was overcome by an oblique incision across the upper abdomen from 9th right to 7th left costal cartilage in line with the outer part of the 5th left interspace.

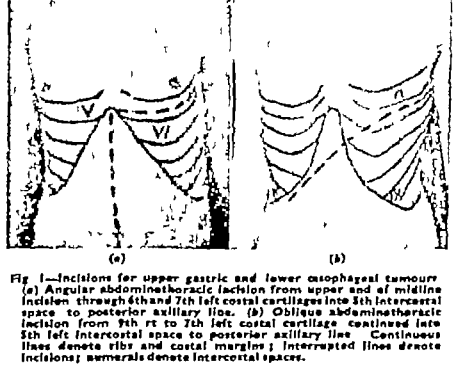

Fig. 1.—Incisions for upper gastric and lower œsophageal tumours. (a) Angular abdominothoracic incision from upper end of midline incision through 6th and 7th left costal cartilages into 5th intercostal space to posterior axillary line. (b) Oblique abdominothoracic incision from 9th rt to 7th left costal cartilage continued into 5th left intercostal space to posterior axillary line. Continuous lines denote ribs and costal margins; interrupted lines denote incisions; numerals denote intercostal spaces.

After the abdomen has been explored through this incision, the incision can be continued through the left costal margin lower down into the 5th space (fig. 1b); the thorax opened, and the diaphragm divided as before. This gives a wide straight opening with much better direct access to the whole stomach and lower œsophagus.

(2) *For Mid and Lower Abdominal Visceral Cancers*.—A midline incision was used here, as for carcinoma of pancreas (case 8), and extended by a transverse incision as for carcinoma of descending colon (case 9).

(3) *For Upper and Mid thoracic Œsophageal Cancers*.—Approach has been entirely from the thorax through the 5th left interspace for the mid thoracic part of the œsophagus, and through the 3rd or 4th right interspace for the upper thoracic part. The ribs above and below the space selected are divided subperiosteally at each end to allow of wider opening than that usually required for surgery alone, enabling the glandular field in the mediastinum to be irradiated.

ANÆSTHESIA

Preoperative medication has usually been with 'Omnopon' and scopolamine. During the first 12 months basal anæsthesia was obtained with gas-and oxygen supplemented with a little ether, changed to chloroform while in the radiotherapy room. Recently 'Pentothal' by continuous intravenous infusion was substituted for the ether and chloroform. Muscular relaxation was obtained with a field block with 'Anethaine' and an anterior splanchnic block was used when possible.

OPERATIVE PROCEDURE

(1) *Exploration of the tumour and field of local spread* by laparotomy or thoracotomy, which helps confirm the diagnosis; biopsy may complete it.

(2) Exploration of the whole abdomen or thorax for widespread metastases, which rule out irradiation as a curative measure.

(3) Measurements of the tumour are noted with its relations to other viscera, and the degree and type of spread in each direction.

(4) Consultation between surgeon, radiotherapist, pathologist, and anæsthetist to decide whether the lesion

is (*a*) operable; (*b*) inoperable, but suitable for curative direct irradiation, (*c*) suitable for palliative direct irradiation only, (*d*) suitable for palliative operation only, (*e*) unsuitable for any treatment

(5) Where direct irradiation is contemplated, extension of the incision may be necessary, as described above

(6) Where indicated, operations to relieve obstruction—e g, gastrojejunostomy and gastrostomy—are done before the irradiation, when possible in an area of stomach not to be irradiated Such a large dose of irradiation might delay the firm healing of the anastomosis, with subsequent leakage and peritonitis

(7) Isolation of the tumour in the open wound, displacing normal viscera by retraction and packing, to minimise the irradiation of normal tissues

(8) Sterilised oiled silk or transparent rubber sheeting protects the field against infection during irradiation but allows accurate visual centring of the tumour in the X-ray beam. Lead screening is applied to the skin edges when necessary

(9) The patient is then given the predetermined dose of irradiation in the radiotherapy room, and returned to the theatre for closure of the wound - To avoid shock produced by frequent moving, a special trolley has been designed on which the patient can have both the operation and the direct irradiation

A BRIEF SUMMARY OF RADIOLOGICAL DATA

Apparatus—The apparatus consists of two Metropolitan Vickers constantly evacuated X-ray tubes of the 250 kv type Special modifications in the lay-out and in various components of this apparatus have been made, so that both tubes may be used simultaneously in treating a single lesion. This has been done to increase the lesion intensity to double that available with the standard apparatus The lower tube has a vertical traverse only, whereas the overhead tube has a vertical and a horizontal traverse The beam of each tube can be rotated through 300° in a vertical plane Using radiation giving a HAV of 1 7 mm Cu, the available surface intensity is of the order of 1000 r/m, and with radiation of HAV 2 05 mm Cu 720 r/m, from each tube In each case the FSD is 21 7 cm and field 13 cm diameter

Method of Use—In our original method one tube only was used to administer a single dose of irradiation directly to the lesion through a parietal opening at the time of operation This was followed in 10–14 days by a further dose given through the skin to make up for the fall in value of the original dose owing to depth In our later cases the above method was modified in an attempt to give an adequate total dose of irradiation at one exposure, with more uniform distribution, and by so doing to eliminate the necessity for subsequent external irradiation For this purpose the applicator of the overhead tube would be in contact with the anterior surface of the tumour, and the lower tube, the X-ray beam being directed upwards, would be below the radiotherapy table, irradiating the posterior surface of the lesion through the skin, the central ray of each beam being so directed as to pass through the centre of the lesion The arrangement of the tubes in use is shown in fig 2

In the first method, using one tube only for the open irradiation, the quality of radiation gave HAV 1 7 and 2 05 mm Cu in different cases Surface lesion intensity varied between 288 and 1000 r/m in different cases. Focus lesion distance was 21 7–40 cm in different cases Field sizes were from 10 × 8 cm rectangle to 13 cm diameter circle Depth dose has been 32%–35% at 10 cm. Total initial lesion dose through the wound has been 500–1200 r, the latter figure being chosen in the earlier cases because it had proved effective in certain superficial lesions. Also it was thought that a larger dose might cause massive necrosis of tumour tissue, with a risk of hæmorrhage and perforation.

In the second method a provisional figure of 1300 r was decided on as a minimal dose throughout the tumour, entailing a surface dose of 1350 r from each tube simultaneously All factors used have been as described for the first method

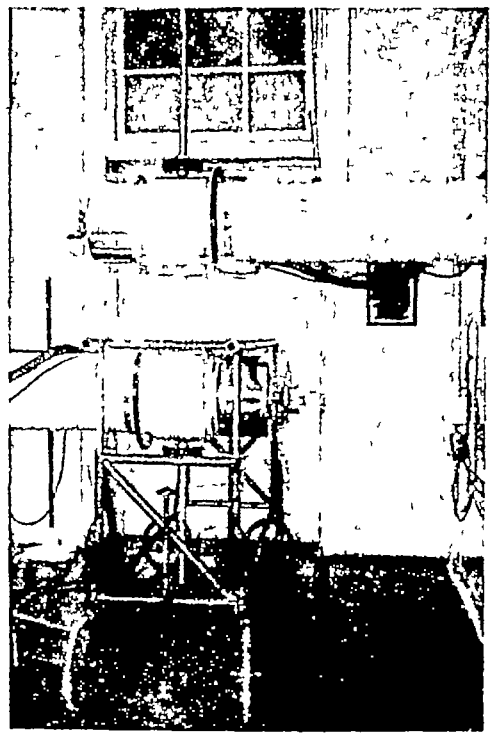

Fig 2—View of the two X-ray tubes and special trolley in position for direct irradiation as described in our second method This trolley was designed to enable both operation and irradiation to be carried out without moving the patient, from the time of leaving to the time of returning to the ward Canvas top of stretcher is in contact with the lower tube applicator, and it can be raised as a whole or tilted in any direction

POSTOPERATIVE AND IRRADIATION REACTIONS

Reactions have been no more severe than would have been expected after the operation alone, which often involved extensive exposure of viscera, with both thorax and abdomen widely open together, and much manipulation during isolation of the tumour Even after giving 1500 r in some 3 min there has been remarkably little reaction, which has come on later, when the operative shock has passed off, and was limited to slight nausea and anorexia, there being rarely any vomiting Blood changes have been less severe than usually found after external irradiation, when the dose is spread over a longer time and a far greater volume of tissue is treated. Irradiation reaction has been more severe and the recovery much slower after the external irradiation, given to some of our earlier cases some months after the operation and direct irradiation, even though the patients were generally more fit when they had the external irradiation, which was a relatively smaller dose spread over a few weeks

CASE-RECORDS

During the past 18 months 15 cases of all types of visceral cancer have been treated In 6 of these, comprising cancers of the stomach (3), œsophagus (2), and colon (1), treatment was purely palliative, because the disease had spread beyond the possible field of irradiation Little beneficial effect was achieved in this group Of the other 9, comprising cancers of the stomach (6), abdominal œsophagus (1), pancreas (1), and colon (1), details are as follows

CASE 1—A man, aged 35, with carcinoma of stomach (lesser curve) Laparotomy, Feb 15, 1944, via upper midline incision, widened by division of both lower costal margins. Tumour a large elongated flat plaque extending from 2 5 cm short of pylorus to cardia, stony hard surface, irregular, with subserous spread. Measurements 13 cm vertically, 7 cm anteroposteriorly, and 4 5 cm thick. Rest of stomach normal No spread to glands or viscera Biopsy not made, but surgeon, radiotherapist, and pathologist all sure of diagnosis

Tumour irradiated with one tube Maximal tumour dose 1000 r in 1 min External irradiation begun 9 days later, amounting to maximal tumour dose of 970 r in 12 days Total maximal tumour dose 1970 r in 1[illegible] days Progress to Aug 22, 1945 decreased very much in size, with tumour some contraction of stomach also, patient gained over 2 stones weight since operation, appetite good, no dyspepsia, eats anything blood condition satisfactory, working for last 12 months

CASE 2—A man, aged 60 with carcinoma of stomach (greater curve) Laparotomy April 4, 1944 via upper midline incision Tumour a large irregular stony-hard mass on greater curve in pyloric antrum measuring 13 cm transverse

7 cm vertically and 7·5 cm anteroposteriorly, with an ulcer 7·5 cm across facing into lumen of stomach. Tumour attached to and invading pancreas. Subserous spread on surface of tumour; some removed for biopsy. Reported as large spheroidal and round-celled adenocarcinoma of stomach with well marked mucoid change. No other spread found.

Tumour irradiated with one tube. Maximal tumour dose 1000 r in 1·5 min. External irradiation begun 9 days later amounting to maximal tumour dose of 991 r in 6 days. Total maximal tumour dose 1991 r in 16 days. Progress to Nov. 23, 1944: complete relief of pain since operation; general condition good; appetite good; gained 1½ stone in weight; working for past 2 months.

Readmitted Nov. 23 for further external irradiation, because it was thought that the initial dose was too small, to cure lesion. Second maximal tumour dose 2640 r in 8 days. Progress to June 17, 1945: reaction more severe and recovery slower; general condition fair and still improving; eating well; gaining weight.

The patient subsequently died suddenly and at the necropsy no macroscopic evidence of new growth was found in the treated area, but some was found outside it.

CASE 3.—A man, aged 67, with carcinoma of stomach (pyloric antrum). Laparotomy Feb. 22, 1944, via upper midline incision. Tumour a hard irregular cylindrical mass encircling pylorus and pyloric antrum, 6·5 cm long and 5 cm across. Glands in lesser curve taken for biopsy. Reported as early infiltration of gland with carcinoma cells compatible with stomach primary carcinoma.

Tumour and glands irradiated with one tube. Maximal tumour dose 1000 r in 1·5 min. External irradiation begun in 9 days, stopped after a few days (275 r maximal tumour dose) owing to development of lung abscess. External irradiation begun again 6 weeks later with a further 1089 r. Total maximal tumour dose 2364 r in 56 days. Progress: almost complete pyloric obstruction developed owing to fibrosis and contraction in tumour after irradiation. No improvement took place by May 30, 1944, so gastrojejunostomy was performed. Patient died of heart failure within a week.

The second operation could have been avoided, had a short circuit been done at the first operation, though the patient was in poor condition then. The irradiation given was inadequate, but a larger dosage was precluded by the patient's poor condition.

CASE 4.—A woman, aged 57, with carcinoma of abdominal œsophagus. Angular abdominothoracic incision on May 16, 1944. Abdomen explored. Small stony hard pear-shaped tumour encircling abdominal œsophagus 5 cm long × 2·5 cm across. No signs of spread. Incision continued into thorax. No spread in thorax.

Tumour irradiated with one tube. Maximal tumour dose 1000 r in 4·20 min. External irradiation begun in 9 days, amounting to a maximal tumour dose of 2541 r in 11 days. Total maximal tumour dose 3541 r in 20 days.

Progress to Feb. 6, 1945, very satisfactory. Swallowing greatly improved. Gaining weight. Further external irradiation to cover whole length of mediastinum and lesser omentum begun on March 12. Maximal tumour dose 2040 r in 4 days. Severe general reaction. Progress to July 22: general condition improving, gaining weight, swallowing almost normal, blood condition satisfactory.

This patient subsequently died suddenly and at the necropsy no macroscopic evidence was found of new growth anywhere in the thorax or the abdomen.

CASE 5.—A woman, aged 46, with carcinoma of stomach (lesser curve). Laparotomy on Nov. 21, 1944, via upper midline incision. Saddle-shaped tumour on lesser curve in pyloric antrum and body, 8 cm. transversely × 5 cm. vertically × 4 cm. thick. Hard glands along lesser curve and below pylorus and body of pancreas. Biopsy of glands showed infiltration by mucus secreting carcinoma, showing little differentiation and increased fibrous stroma as in leather bottle stomach.

Tumour and glands irradiated by two tubes. Maximal tumour dose 1528 r in 2·4 min. Patient stood operation and irradiation very well but suddenly collapsed and died just as the wound was being closed. Autopsy showed complete collapse of both lungs, for which no cause either intra- or extra-pulmonary was found.

This was the first case in which two tubes were used together, but it was felt that this alone could not have caused death. The other factors of operation and anæsthesia were the same as formerly.

CASE 6.—A man, aged 68, with carcinoma of stomach (cardia). Oblique abdominothoracic incision on Feb. 13, 1945. Abdomen explored. Tumour at cardia 6 cm. transversely × 4 cm. vertically and 3·5 cm. anteroposteriorly. Glands in lesser curve and above cardia. No spread elsewhere in abdomen. Biopsy of glands showed poorly differentiated adenocarcinoma invading lymph gland. Incision continued into thorax. No spread in thorax.

Tumour and glands irradiated with two tubes. Maximal tumour dose 1190 r in 1·8 min., smaller than intended as lower tube became unstable and was turned off. Patient progressed very well for 6 days, when spontaneous pneumothorax suddenly developed on right side for no apparent reason, causing rapid death from heart failure in spite of all attempts at resuscitation.

CASE 7.—A woman, aged 54, with carcinoma of stomach (*lesser curve*). *Oblique abdominothoracic incision on March* 23, 1945. Abdomen explored. Saddle-shaped tumour high on lesser curve, extending quarter way round lumen on each surface; stony-hard, nodular with subserous spread, measuring 8 cm. transversely × 4 cm. vertically × 4 cm. anteroposteriorly. Glands along lesser curve. Biopsy showed moderately differentiated adenocarcinoma with much fibrous stroma invading lymph gland. No other sign of spread. Incision continued into thorax.

Tumour and glands irradiated with two tubes. Maximal tumour dose 1542 r in 3 min. Progress to July 24: general condition good and improving; no dyspepsia; appetite good; eating full diet; gaining weight; blood condition satisfactory.

CASE 8.—A woman, aged 60, with carcinoma of pancreas (body). Laparotomy on May 16, 1944, via midline incision. Stony hard mass in body of pancreas 5 cm. × 5 cm. No signs of spread. Biopsy of pancreas showed adenocarcinoma.

Tumour treated with one tube. Maximal tumour dose 750 r in 1·5 min. External irradiation begun in 9 days. Total maximal tumour dose 3010 r in 21 days. Progress to Aug. 4, 1944: condition much improved; all pain relieved, gained some weight.

Returned to hospital on Oct. 30 for follow-up. Ascites. Indefinite mass felt in abdomen after paracentesis abdominis. Further external irradiation begun Nov. 9. Maximal tumour dose 2475 r in 14 days. Patient gradually deteriorated and died on Dec. 8. Autopsy showed complete disappearance of original tumour, palpable mass being scar tissue and *adherent bowel but wide spread metastases outside this* area in liver, peritoneum, and para-aortic glands.

This being an early case in the series, the original tumour dose of irradiation was small, and only one tube was used, but her condition had been definitely alleviated although she died from wide-spread metastases which probably had developed before treatment began.

CASE 9.—A woman, aged 67, with carcinoma of colon (descending). Laparotomy on Jan. 23, 1945, via lower midline incision. Large hard fixed mass in left iliac fossa *firmly adherent to peritoneum, attached to bladder at lower* end, completely encircling colon, measuring 9 cm. long, 6 cm. wide, and 6 cm. deep. No sign of spread. Right transverse colostomy performed through separate upper paramedian incision. Midline incision extended transversely to left iliac crest giving direct exposure of tumour. Tumour irradiated with two tubes. Maximal tumour dose 1560 r in 2·5 min. Progress to Aug. 28: general condition very good; gained 14 lb. in weight since operation; no symptoms; no tumour palpable in left iliac fossa.

CONCLUSIONS

Although the series is small, we feel sure that our method will prove to be a rational and hopeful advance in the treatment of inoperable cancer of viscera. Whether the cancer is rendered inoperable by the poor general condition of the patient or by irremovable local spread, this method will often succeed where surgery alone must inevitably fail. Though wider exposure is needed than for surgery alone, with adequate precautions the whole procedure should not be so shock producing as is wide surgical excision. Exploratory operation is the only reliable way of deciding the correct form of treatment, and the hospital of the future will have a radiotherapy room adjoining the operating theatre to facilitate direct irradiation.

It is more reasonable to irradiate most what most needs irradiating—i.e., the tumour and field of local spread—and not the overlying skin or intervening vital tissues. There being no precedent to indicate the probable effects of such high tumour doses given within a minimum of 2–5 min., we have given in the earlier cases rather smaller doses than could be expected to be curative alone, so these patients have had supplementary external irradiation beginning within 10 days of operation. Some have had further external treatment again later.

We have gradually increased the initial dose and now use two tubes together. We hope eventually to be able to give an adequate initial dose so as to dispense with the routine external irradiation. But, until we have more experience in the relation of radiosensitivity to the microscopic and macroscopic types of cancer, it will still remain a most difficult problem to decide for or against further external irradiation.

Biopsy may not be practicable in all cases, being not altogether devoid of risk when there is no obvious glandular spread. But even biopsy is not always reliable, for surgeons and radiotherapists have too often been misled by them in the past. Being able to see and feel the tumour should make the diagnosis more certain than when relying on external methods of examination alone, and biopsy will often increase that certainty. Autopsy is perhaps the only way of achieving absolute certainty, and the object of our treatment is to try to postpone that event.

All the patients were bad risks for any operative procedure, and they would all inevitably have died within a few months at most if untreated. Now 5 are doing well at over 18 months, 15 months, 15 months, 7 months, and 5 months after combined operation and irradiation. Though our methods have failed to palliate other more advanced cases, the experience gained with them has been most valuable in leading to modifications and improvements in technique in many directions. No doubt further changes will be necessary as we progress.

Being a new method of treatment it has not been easy so far to obtain a sufficient number of suitable cases to give it a fair trial. Some were too far advanced for exploration and treatment, and some others were found to be operable and were treated surgically. We have written this paper to show that our method is a reasonable and practicable possibility, which we feel sure will lead to an increase in the cure-rate of these hopeless cases; and to appeal for more cases.

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"If a Government is offering to the people of the country a 100 per cent pharmaceutical and medical service costing a very large sum of money every year there is no justification for the daily papers and the hoardings telling the people of the country that they need not make use of the Service the Government provides but can choose their own illness from a list provided in the advertisement."—HUGH N. LINSTEAD, MP. *Pharmaceut. J.*, Sept. 29, 1945, p. 141.

INFLUENCE OF TEMPERATURE ON SEDIMENTATION-RATE

ITS CLINICAL SIGNIFICANCE

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MOST textbooks say that high external temperature accelerate and low ones retard the red-cell sedimentation rate (SR), but our experience in Bikaner, where since 1938 the SR has been tested as a routine in all medical cases, led us to doubt the accuracy of this statement. The room temperature in our laboratory during working hours is about 98° F in May and 60° F or a little less in January, the seasons change quickly. SR done at different periods in some cases did not conform to the rule, so we investigated the matter more closely.

METHOD OF INVESTIGATION

Westergren's method was used with all technical precautions. The readings were taken every ten minutes. Blood was withdrawn with as little venous stasis as possible, the patient having been kept fasting. Two SR determinations were carried out simultaneously, one at 99° F, the other at 44° F. These temperatures are conveniently obtainable in every laboratory in an incubator and a refrigerator respectively. In a sufficiently large number of cases (the first 200 of our series) the blood was divided and kept for an hour at 99° F and 44° F, and after thorough shaking two tubes were filled with chilled and two with warm blood. One of each was then put into the cold and hot compartments. Except for a very slight deviation in the first minutes, previous chilling or warming did not affect the SR. Special care was taken to conserve steady conditions, and the doors of the chambers were opened for a few seconds only every ten minutes.

Cases showing a higher SR at 99° F are marked SR +. Cases showing no appreciable difference (up to 10%) at any stage during an hour are marked SR 0. Cases showing a higher SR at 44° F are marked SR −.

RESULTS

Of 483 cases examined in this way 279 (57·7%) showed SR +, 109 (22·7%) SR −, and 95 (19·7%) SR 0, they are divisible into three groups.

Group I.—This comprised respiratory (including uncomplicated pulmonary tuberculosis), circulatory, digestive, nervous, and skin diseases, gonorrhœa, arthritis, &c., and consisted of 252 cases, 198 ~~showing~~ SR + and 54 SR 0. Six cases of ascites with SR + appear in this group, three of them were cancer of the peritoneum, one primary tuberculous peritonitis, one Pick's disease, and one chronic portal thrombosis.

Group II.—The SR varied in this group, details are given in table I.

Group III.—This group always gave SR − and consisted of the following cases:

	Cases
Atrophic cirrhosis of liver	19
Kala azar	9
Amœbic liver abscess	6
Pulmonary tuberculosis with intestinal tuberculosis	3
Primary intestinal tuberculosis	4
Cancer of the liver (one primary, two metastatic)	3
Subacute icterus gravis	2
Arsenical hepatitis	1

Only 1 of the 19 patients with atrophic cirrhosis of the liver was a regular and fairly heavy drinker. The other 18 were either abstemious or took alcohol very rarely, and in small quantities. All of them habitually ate strongly spiced food.

In group III the SR was most pronounced, readings for the first 10 min. often being more than five times higher in the cold than in the warm. A few typical instances are given in table II. In the cold the fall of the corpuscles was very rapid during the first 30 min. The SR slows down only as packing of the corpuscles prevails. In all these cases, the clumping of RBC into large visible aggregates was very remarkable, usually already a few minutes after the tube had been placed in the refrigerator.

This phenomenon was very pronounced in a case of blackwater fever where, immediately after the sedimentation tube had been filled with citrated blood, the whole column took on a granular appearance and large clumps of RBC could

seen quickly falling to the bottom of the tube The sedimentation was completed in under 2 min A similarly rapid SR has not been noticed in any other case Bikaner is free from blackwater fever (this case came from Bengal), and the SR in blackwater fever could therefore not be further investigated This observation was made before we began to compare SR methodically in the heat and the cold

TABLE I—SR IN DISEASES OF GROUP II

Disease	Cases	SR +	SR 0	SR −
Malaria	122	47	29	46
Amœbic hepatitis	5	1	—	4
Catarrhal jaundice	5	2	2	1
Diabetes	7	4	2	1
Microcytic anæmia	7	2	3	2
Acute (bacillary) dysentery	9	2	4	3
Chronic colitis	9	6	1	2
Typhoid	5	1	—	1
Syphilis (primary and secondary)	15	13	1	1

In some cases the SR before treatment could be compared with the SR after clinical cure A few instances are given here In a case of arsenical hepatitis in primary syphilis treated with neoarsphenamine and bismuth, after 2 1 g of neoarsphenamine the patient developed jaundice, fever, and drowsiness. Details of the SR on admission, at the height of clinical symptoms, and after cure with sodium thiosulphate and insulin glucose are given in table III Similar details are given in table IV (A and B) for amœbic hepatitis before and after treatment with emetine and for malaria, of 3 months' duration, before and after treatment with quinine

TABLE II—EXAMPLES OF SR IN DISEASES OF GROUP III

Cirrhosis of liver		Kala-azar		Amœbic liver-abscess		Intestinal tuberculosis		Cancer of liver	
99 F	44 F	99 F	44 F	99° F	44 F	99 F	44 F	99° F	44° F
5	49	7	20	23	40	4	6	15	70
11	75	18	103	63	112	11	30	40	103
10	84	25	111	73	113	18	65	60	108
27	91	32	113	89	117	25	79	80	112
35	98	41	115	101	120	32	89	92	119
48	104	52	116	121	124	40	99	98	123

DISCUSSION

It appears that the SR — is closely associated with hepatic disorders Very pronounced acceleration of the SR in the cold was obtained in all 10 cases of atrophic cirrhosis, which is considered the prototype of advanced parenchymatous degeneration

All 9 cases of kala-azar had an even more rapid fall during the first 30 min, reaching the stage of almost complete packing at the end of this period In one autopsy histological changes in the liver consisted of atrophy and fatty degeneration of liver-cells, perivascular round-cell infiltrations, and diffuse intralobular cirrhosis In this connexion, it is interesting to note that Chaudhuri and Chaudhuri (1943) in performing the Takata test in 120 cases found in 6 cases of cirrhosis 1 positive, 1 doubtful, and 4 negative; and in 44 cases of kala-azar 10 strongly positive, 16 positive, 5 doubtful, and 4 negative results.

In 1 case of arsenical and 2 cases of subacute necrosis of liver, which were all cured with insulin-glucose, the SR could be compared well with the clinical symptoms With the onset of jaundice in the case of arsenical hepatitis sedimentation was still higher in the heat, and only when drowsiness and delirium were pronounced did the SR show a definite increase in the cold, most distinct on the 11th day, when general toxæmia was already lessening After clinical recovery, with only slight icteric discoloration of the sclerænd no bilirubin in the urine, it took another 10 days for the SR to return to its normal higher fall in the heat The 2 cases of subacute necrosis, which were admitted with already fully developed signs, showed a similar reversal on recovery

All 7 cases of pulmonary tuberculosis with intestinal tuberculosis and primary intestinal tuberculosis, had cachexia, anæmia, and œdema No autopsy could be done in any of these cases, but presumably diffuse fatty degeneration of the liver was present

The 8 cases of cancer had enormously enlarged livers with gross nodular irregularities of the surface The destruction of liver tissue in these cases must have been considerable

In group II only one autopsy could be performed The patient with typhoid, with SR −, died from perforation and peritonitis. The liver presented a typical picture of cloudy swelling and focal necrosis.

Amœbic hepatitis showed SR — in 4 out of 5 cases The cytolytic action of the ferment or toxin of the amœba on the liver where it is conveyed through the portal bloodstream may be accepted as a possible explanation

In all other cases the cause for SR — cannot be equally well determined. In bacillary dysentery toxins or even bacilli may reach the liver tissue In chronic colitis absorption of bacilli or toxic proteolytic products into the portal vein may take place causing liver damage This, however, is only conjecture

TABLE III—30 MINUTE READINGS OF SR IN ARSENICAL HEPATITIS

On admission		At height of symptoms		After cure	
99 F	44° F	99 F	44 F	99° F	44 F
4	2	5	10	2	1
11	4	22	50	7	2
20	6	42	92	15	3

The large proportion of SR — in malaria cases was surprising, being greatest in cases which had gone untreated for over two weeks In our series, 68 cases had no previous medical attendance; 28 of them had their first attack of fever less than fifteen days before admission Of these, 21 showed SR +, 3 SR —, and 4 SR 0 Of 40 untreated cases with over two weeks' history, 31 had SR — and 6 SR + We had no opportunity to perform an autopsy in any of these cases Many of our cases were extremely massive infections observed during an epidemic outbreak of malaria August–November 1942

TABLE IV—30-MINUTE READINGS OF SR IN (A) AMŒBIC HEPATITIS AND (B) MALARIA

Case	(A)—*Amœbic Hepatitis*				(B) *Malaria*			
	On admission		After cure		On admission		After cure	
	99 F	44° F	99° F	44 F	99° F	44 F	99 F	44 F
1	4	6	1	1	15	23	11	3
	10	30	2	1	45	78	30	8
	20	6	5	3	79	105	59	12
2	12	18	5	3	5	30	6	2
	38	55	18	11	18	51	21	10
	65	82	32	21	30	65	33	24

From 1939 to 1941 the rains had failed in Rajputana leading to famine in the whole of the non-irrigated part of the State With early and heavy rainfall in 1942 malaria spread rapidly particularly since systematic quinine prophylaxis could not be undertaken Most of these malaria patients were at the onset emaciated owing to semi-starvation, and there can be little doubt that they had long been deficient in glycogen, which may also explain the unusually high incidence and severity of malaria

Hæmosiderosis of the liver and the clogging of small vessels by parasites, dead endothelial cells and RBC with

consequent focal degeneration of liver-cells, is suggested as the pathological basis of SR —.

Amœbic and bacillary dysentery, besides malaria, have from time to time been held responsible for the large incidence of non-alcoholic atrophic cirrhosis in hot countries If as we believe SR — indicates liver-cell damage, additional weight is given to this theory, because persistent or repeated injury to the parenchyma, followed by repair, will finally lead to atrophic cirrhosis

The diseases in groups II and III were naturally accompanied sometimes by severe anæmia Anæmia per se, however, is not the cause for SR —. The typical secondary (post-hæmorrhagic) anæmia always shows a definite SR + Besides the clinical evidence, SR of different proportions of plasma and corpuscles of SR + and SR — cases were determined Bloods of SR + cases will always give SR +, however low the hæmatocrit value is chosen SR — bloods will always give SR — even with a hæmatocrit of 50% The usual slowing down of the SR with high concentration and speeding up with low concentration of RBC could, as expected, be shown

Investigations to discover the causes responsible for SR — in cases of liver damage are in progress It is likely that protein fractions, particularly globulin and fibrinogen, effect a clumping together of RBC more in the cold than in the heat, which results in very rapid SR —

CONCLUSION

The general statement that SR are higher in warm temperatures is not correct

In certain cases SR is much higher in the cold, a condition denoted here as SR —

SR — appears to be associated with damage to the parenchyma of the liver

The simultaneous examination of SR in warm and cold temperatures seems to have a considerable diagnostic and prognostic value.

I wish to thank Dr Jagdish Chandra, of the Bikaner Clinical and Research Laboratory, for his technical assistance

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CLINICAL TRIALS OF β-PETHIDINE

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PETHIDINE ('Demerol,' or ethyl 4-phenyl-1-methyl-piperidine 4-carboxylate) has now had an extended clinical trial, and there can be no doubt about its efficacy as an analgesic Battermann and Himmelsbach (1943) have given the clinical advantages of pethidine over morphine as its relief of spasm of smooth muscle; its rapid dissipation which tends to offset undesirable cumulative effects, such as respiratory depression and urinary retention; and its lesser liability to produce habituation and physical dependence

On the other hand, we have found that pethidine has a variable action in the control of deep-seated pain Sometimes effective, in other cases it gives the patient little or no relief According to Battermann (1943), side-effects occur in 25% of cases when pethidine is used parenterally in therapeutic dosage Dizziness is the common symptom; occasionally there may be nausea or even vomiting We were therefore glad to test the efficacy of a new analgesic compound, ethyl 3-phenyl-1-methyl-piperidine-3-carboxylate, hereafter referred to as β-pethidine (cf. Bergel et al 1944)

METHOD OF COMPARING ANALGESIC ACTION

The Hardy, Wolff, and Goodell (1940) apparatus measures pain thresholds and employs heating of the skin as a source of pain Slaughter and Wright (1944), using a modified Hardy-Wolff-Goodell machine, found the greatest possible error, in a series of pain-threshold determinations in normal subjects, expressed as a percentage of the mean, to be 1 53 Statistically, therefore, the method is sound It has been used by Barlow (1943) for comparing the analgesic properties of morphine, codeine, and pethidine Barlow found that 125 mg. of pethidine approached the effectiveness of 15 mg of morphine in analgesic action but did not persist so long.

An objection to thermal methods of producing pain in a comparative study of analgesics is that, clinically, pain is not often produced by heat but by other mechanisms A further objection is the complexity of the apparatus

Mechanical contrivances have been used by von Frey (1897) and Eddy (1932) to produce pain by pressure, and we made experiments with the apparatus illustrated (see fig. 1) A screw drives a blunt point into the upper part of the tibia. The blunt point is attached to a

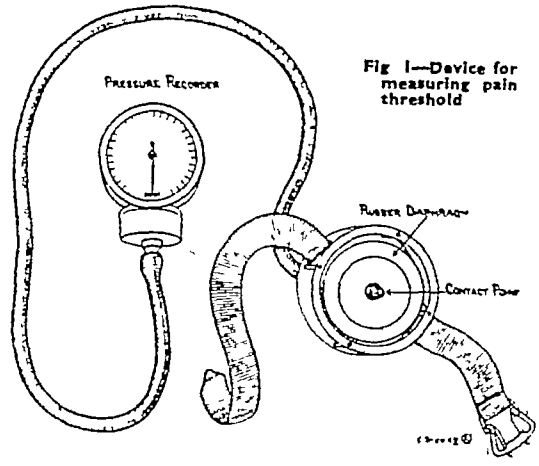

Fig 1—Device for measuring pain threshold

rubber diaphragm, and the pressure is communicated to an ordinary sphygmomanometer gauge by rubber tubing A reading in mm Hg is taken when the subject complains of pain

During the course of a day 10 estimations of the pain threshold were made on each of 8 patients In any one patient only slight variations were obtained in the 10 readings; in fact, the greatest standard deviation was ± 2 2 Thus the greatest probable error expressed as a percentage of the mean was only 0 5 The method promised to be as sound as that employed by Slaughter and Wright (1944), and this simple device was used for comparing the analgesic actions of pethidine and β-pethidine

EXPERIMENT

Six groups of 20 subjects each were treated on different days in one of four ways (*a*) 2 "coco" tablets (each containing aspirin gr 2, phenacetin gr. 2, codeine gr. $\frac{1}{12}$), (*b*) 100 mg pethidine subcutaneously, (*c*) 100 mg β-pethidine subcutaneously; or (*d*) no medication at all

Estimations of the pain threshold were made on group 1 a quarter of an hour after medication, group 2 half an hour, group 3 an hour, group 4 two hours, group 5 three hours, and group 6 four hours, after medication The observer did not know whether any given subject had been treated or not The results are shown in figs 2 and 3

RELATIVE ANALGESIC ACTIONS

Fig. 2 shows the total number of cases in which the pain threshold was altered Every subject receiving either pethidine or β-pethidine showed a raised pain threshold two hours after injection, but the effect of β-pethidine subsided more rapidly than that of pethidine

Fig 3 shows the average raising or lowering of pain threshold, as recorded in mm. Hg at quarter, half, one, two, three, and four hours after medication Maximal effects of both pethidine and β-pethidine were recorded two hours after injection, again pethidine had a longer action thereafter than had β-pethidine. Two "coco" tablets, which we have often seen prescribed in hospitals, had little or no analgesic action

CLINICAL EFFECTIVENESS

Beta-pethidine was found to be a useful analgesic in various painful conditions in a dose of not less than 100 mg It afforded quick relief in intestinal, biliary, and renal colic Particularly gratifying results were noted in three cases of painful flexor spasms associated with advanced disseminated sclerosis and with syringo-

myelia In these conditions its action was similar to that of pethidine, and it was hardly possible from clinical observation to determine any difference in the antispasmodic properties of the two compounds Like pethidine, β pethidine had a curiously variable and unpredictable action in cases of deep-seated and chronic pain Successful in one of two clinically similar cases of severe headache associated with intracranial tumour, it did not relieve the headache of a subarachnoid hæmorrhage Great relief was experienced in cases of sarcoma of the tibia, and of multiple secondary neoplasms in bone, and in a case of gross lumbar osteo-arthritis with severe root-pains. On the other hand, a case of sciatica, and another of sarcoma of the diaphragm gained no benefit whatever from β-pethidine In general, where the pain was such that it was not amenable to ordinary pethidine, β-pethidine also had no effect.

In this group of cases pethidine in equal dosage had a longer and more powerful action than β pethidine, and in one case of a mediastinal neoplasm relief was regularly obtained from the injection of pethidine but not from β pethidine

SIDE-EFFECTS AND TOXICITY

Two patients complained of slight dizziness soon after injection. No complaints of nausea or vomiting were made One patient four hours after a subcutaneous dose of 200 mg complained of paræsthesiæ in all four limbs, followed a little later by severe headache, which persisted for two hours. This incidence of less than 1 6% of unpleasant side-effects compares with Battermann's figures, previously quoted of a 25% incidence of side-effects when ordinary pethidine was used parenterally We have not, however, used the drug in such

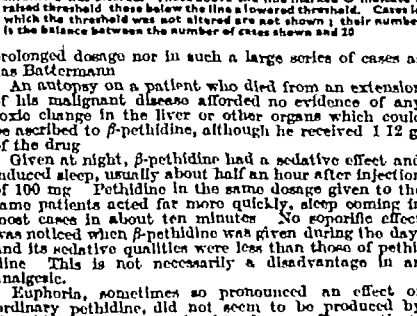

Fig 2—Number of cases, in each group of 20 subjects in which the pain threshold was altered. Those above the line marked O indicate a raised threshold those below the line a lowered threshold. Cases in which the threshold was not altered are not shown; their number is the balance between the number of cases shown and 20

prolonged dosage nor in such a large series of cases as has Battermann

An autopsy on a patient who died from an extension of his malignant disease afforded no evidence of any toxic change in the liver or other organs which could be ascribed to β-pethidine, although he received 1 12 g of the drug

Given at night, β-pethidine had a sedative effect and induced sleep, usually about half an hour after injection of 100 mg Pethidine in the same dosage given to the same patients acted far more quickly, sleep coming in most cases in about ten minutes No soporific effect was noticed when β-pethidine was given during the day, and its sedative qualities were less than those of pethidine This is not necessarily a disadvantage in an analgesic.

Euphoria, sometimes so pronounced an effect of ordinary pethidine, did not seem to be produced by β pethidine to any noticeable degree Two patients developed some emotional lability, but it was difficult to ascribe this to the β pethidine; both had chronic malignant disease Neither patient, after a total dosage of 1 12 g., evinced any withdrawal symptoms. This difference between the two pethidines raises the possibility that β-pethidine will be even less likely than ordinary pethidine to cause addiction. Further experience of this not unimportant aspect of β pethidine is desirable

SUMMARY

Animal tests of a new analgesic drug β pethidine (ethyl 3-phenyl 1 methyl piperidine 3-carboxylate), the application of heat being used for testing the pain threshold, had suggested that its action was similar to that of ordinary pethidine, though it lasted longer (cf Macdonald et al 1945)

With a mechanical method of testing the pain threshold on human subjects it was found that the action of

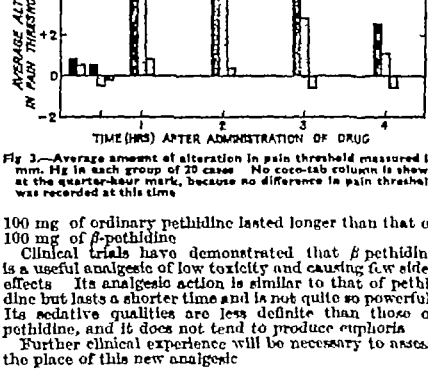

Fig 3.—Average amount of alteration in pain threshold measured in mm. Hg in each group of 20 cases No coco-tab column is shown at the quarter-hour mark, because no difference in pain threshold was recorded at this time

100 mg of ordinary pethidine lasted longer than that of 100 mg of β-pethidine

Clinical trials have demonstrated that β pethidine is a useful analgesic of low toxicity and causing few side-effects Its analgesic action is similar to that of pethidine but lasts a shorter time and is not quite so powerful. Its sedative qualities are less definite than those of pethidine, and it does not tend to produce euphoria

Further clinical experience will be necessary to assess the place of this new analgesic

We wish to thank Prof D M Lyon for his help and encouragement The β pethidine was supplied by Messrs. Roche Products Ltd

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'A man wants three houses in his life time one when he gets married, one when the family is growing up and one when he is old I hope the old people will not be asked to live in colonies of their own—after all they do not want to look out of their windows on endless processions of the funerals of their friends they also want to look at processions of perambulators '—Mr ANEURIN BEVAN *Hansard*, Oct 17, 1945 par 1222

'Mental fatigue is akin to boredom, and housing can be made to encourage or alleviate this condition especially in women. Labour-saving devices organisation of work so that successive operations are placed in a continuous sequence adequate lighting, provision of necessities in easily accessible places, and provision of an attractive outlook as well as a pleasing interior are all important means to this end Variety is a useful antidote to mental fatigue Rooms should not all have the same design or finish; houses should pay more than lip service to variation of design A visit to another house should provide a change of material as well as of personal environment Gardens, paths roads, parks public buildings, all play a part in counteracting boredom and in stimulating bodily reactivity " Prof DOROTHEA H. LEE, *University of Queensland Papers Dept of Hygiene* 1944, 1, No 8

Medical Societies

EUGENICS SOCIETY

AT a meeting of the society on Oct. 16, with Dr. AUBREY LEWIS in the chair, a paper on

Mental Health in a Rural Area

was read by Dr. W MAYER-GROSS He is conducting, with the help of a team of psychiatric and social workers, a survey of the mental health of residents in an area near a big Scottish mental hospital, and he described the findings up to the present No survey of this kind—including minor as well as major psychiatric disorders—has been made in Great Britain before, though there have been two in America The methods used were based on those of Strömgren when he surveyed the Danish island of Bornholm, chiefly for major psychoses, in 1938. He lived there, and made touch with doctors, teachers, clergymen, aldermen, officials, and the older residents; and he studied the records of hospitals and almshouses The Scottish survey began with a study of records at the local mental hospital, where patients from the area have been treated for more than 100 years. Inquiries in the area were made by the social worker, who was more able to approach this topic without offence than a doctor would have been. She visited patients discharged from the hospital during the preceding 10 years and the relatives of those still in hospital, through the medical officer of health she made touch with local government, public assistance officers, and sanitary inspectors She visited certified mental defectives, and was given access to schools and teachers and to the results of an intelligence test taken by all school-children at the age of 11 Doctors, ministers, district nurses, welfare and SPCC officers, and police coöperated; and Scottish neighbours as usual proved to be well informed about each other. It was rare to find that nothing at all could be elicited about the personal habits and peculiarities of a suspected case

As an illustration of the results, Dr Mayer-Gross chose a purely agricultural district of 5 parishes, covering about 64,000 acres, with a population of 5041 at the 1931 census The area is not subject to large migrations, and he thinks it likely that the population has remained relatively stable Cases were analysed under 10 diagnoses, some of which include several types of disorder. Thus neurosis in children includes enuresis and stammering, neurosis and psychopathy in adults covers anxiety, obsessional illness, hysteria, aggressive excitable psychopathy, and a tendency to drift.

The incidence of mental defect was high, confirming the experience of E O Lewis, in his study of mental defect in rural areas There were 13 7 mental defectives per 1000 population, a figure higher than Lewis's, and 26 4 per 1000 of dull and backward—people, that is, with an IQ between 70 and 80 Only 4 per 1000 of maladjusted and neurotic children were found. Neurosis and psychopathy accounted for 20 8 per 1000, manic-depressive illness for 2 4, schizophrenia for 4 8, alcohol and other toxic psychoses for 2 4, epilepsy for 1 4, senile and arteriosclerotic psychoses for 3 4; other organic psychoses, with undiagnosed and suspected cases, amounted to 7 6 per 1000 The total number of mentally abnormal cases in the area was 410, or 86 9 per 1000—a figure higher than in the two American surveys Analysis by age-groups showed a high proportion of young people in the dull and defective group, which Dr. Mayer-Gross attributes to the fact that the survey had fuller information about children born after 1926 The age-distribution of the abnormal cases corresponds to that of the population in the district Defectives, and the dull and backward, were more common in the families of unskilled labourers than in the families of higher grades of worker. He noted that the need for treatment was high. 35 needed inpatient and 41 outpatient care, only 10 children were getting special schooling; 64 needed it.

In 120 marriages among the 440 patients there were 9 cases of separation and divorce; and in 25 married couples both partners came under the survey as cases There were only 38 dull and defective among the married, probably because most of the patients in these backward groups are still below the age of 25; but a larger proportion of these patients lived harmoniously with their spouses than did married patients with other types of mental abnormality.

Mr. RICHARD TITMUSS, commenting on the high proportion of dull and defective cases, suggested that some selective factor may be at work inducing the backward to stay in the area, or the brighter to move out. Dr T RUSSELL FRASER asked where the survey drew the line between the normal and the abnormal. The social adjustment of the patient, Dr. Mayer-Gross replied, was the decisive factor.

Reviews of Books

Surgical Disorders of the Chest

Diagnosis and Treatment J. K DONALDSON, MD, FACS, major USAMC (Kimpton Pp 304 33s.)

STUDENTS of thoracic surgery will welcome this book, though it exhibits many minor points of difference from the accepted practice in this country. More emphasis on general principles would have been helpful to the less experienced, especially in the section on treatment of empyema Failure to deal with empyema satisfactorily is one of the chief blots on modern surgery and can only be remedied by rigid attention to both general principles and details. The position of the average drainage opening, the size of the drainage tube, and the control of the healing of the cavity with pleurograms are points which might well have been emphasised; so might the use of breathing exercises to expand collapsed lung

Though all branches of chest surgery are included some sections are outstanding—for example, those on subphrenic abscess, lung abscess, and carcinoma of the œsophagus. Anæsthesia is briefly discussed, but artificial respiration, oxygen administration, and resuscitation are described more fully Major Donaldson has achieved a judicious balance between clinical description, technical detail, and case-reports, and the illustrations are well chosen

Leukopenia and Agranulocytosis

WILLIAM DAMESHEK, MD, clinical professor of medicine, Tufts College, Boston, Mass (Oxford University Press Pp 78 10s 6d.)

THIS is a reprint of the section in the "Oxford Loose-Leaf Medicine," a work now well Americanised. Dameshek's section follows suit by ignoring all British work, but it presents a good detailed summary of the American investigations and mentions those of Preben Plum in Denmark. There is one new point. since agranulocytosis robs the patient of an important part of his anti infection defences, it is logical to treat the severe cases with penicillin or even sulphonamides to combat a possible bacteriæmia, only some agranulocytosis patients show such a widespread bacterial invasion and the reason for the death of the others is still a mystery. Dameshek has come to the same conclusion as most other workers that the value of pentose nucleotide, leucocyte cream, liver extract, yellow bone-marrow, blood-transfusion, and other proposed measures, is very doubtful and that recovery is probably little influenced by them—occurring, in fact, in spite of them Prevention, by constant care when using granulopenic drugs, is all the more important. There is little in this book that cannot be found in the standard hæmatological textbooks

Medical Annual 1945

(63rd year) Editors Sir HENRY TIDY, KBE, DM OXFD, FRCP, A. RENDLE SHORT, MD LOND., FRCS (Wright Pp 410 25s)

THIS medical March of Time continues on its steady course, late but otherwise unperturbed by the events among which it has been produced. This year there is a section on measurement of morbidity, by Prof Ralph Picken; and a new section on vital statistics, by Dr Percy Stocks, is to become an annual feature. Next year perhaps we shall see sections on social medicine, reablement, and industrial medicine. A distinguished American, Colonel W. S. Middleton, contributes a long section on primary atypical pneumonia. Outstanding among other contributions are Dr. Macdonald Critchley's frank discussion of the Kenny treatment of poliomyelitis, and Dr. Ernest Lloyd's judicial summing up of the present status of mass miniature radiography.

THE LANCET

LONDON SATURDAY, OCTOBER 27, 1945

Members of One Another

IN the war years Service doctors have worked with ilian doctors both in and out of uniform The ofession can take pride in their joint achievements e sick and wounded have been tended with devo on, efficiency, and unprecedented success, while e high level of physical and mental health in the orces owes much to an improved practice of pre entive and social medicine

The close association of these two unlike creatures the Service doctor and the civilian doctor—has rought out certain differences of outlook and inion, indeed, some of these have disclosed them lves with explosive force But success in a common ause has created a useful reserve of mutual respect nd good will Now that uniforms are being taken ff, the time has come to forget the differences and rn our thoughts to means of preserving this good ill Prompt initiative is needed, because the English uickly turn their minds from anything connected ith war But in the coming years our sons and aughters may have to enter the Forces in greater umbers than formerly, and the whole profession ust concern itself with the medicine that will be ractised on the nation s youth No longer can the ervices, and Service medicine, be considered some hing separate and apart, and much will be gained f in peace time there is continuous, agreeable, and rofitable association between the civilian doctor nd his military colleague The fact that they lead ery different lives need not induce a feeling of con lescension or superiority on either side

To cement and continue the present alliance etween Service and civilian doctors calls for some nedical EISENHOWER with qualities that will earn qual support and confidence from both parties But it does not require any new or elaborate organisa ion the machinery he would need is already largely n being If we consider for example, the case of he Army which has been far the largest employer of medical officers, it is clear that much could be done hrough the Royal Army Medical College, famous for ts traditions of teaching and research, especially f this college were again affiliated to the University of London During the war there has been close and fruitful contact between the War Office on the one hand and the Medical Research Council, universi ties and medical schools on the other Men of cientific repute have sought and obtained from the military authorities the help they needed for the study of such important problems as traumatic shock, nfective hepatitis poliomyelitis the use of penicillin in war wounds, scrub typhus, and malaria—to name only a few Some of these research workers joined the Army in the ordinary way for the duration of the war, others went into uniform for limited periods during which they were posted from a "research pool" to wherever they could work most profitably Others who remained in civilian clothes have associated none the less fully and usefully with the War Office It may not always have been easy to fit together the researchers, their equipment the opportunity, and the right operational conditions, but remarkable helpfulness has been shown on both sides, and the benefits of success have been shared A similar story can be told of the Royal Navy and the Royal Air Force, and it is obvious that in the uneasy peace that lies ahead of us the same kind of association must go on, and in fact be increased

But there is also another opportunity for joint effort—namely, postgraduate study Why should not the medical services of the Armed Forces extend their admirable arrangements so that "study duty" comes round not once in an officer s career but regularly? Just as there has been a research pool to help civilians into a Service for limited periods, so there should be a training pool from which Service medical officers could be posted to hospitals and universities for frequent and substantial periods of training, experience, and possibly research In the tropics it is only an exceptional officer that is likely to give much of his free time to study, but on each return to these islands all should revive their professional outlook by close contact with those whose interest is the advancement of knowledge and the improvement of practice Under present conditions of promotion, which stand in great need of revision, the Service doctor naturally aims at becoming an administrator, but he cannot administer efficiently unless he keeps in touch with professional thought and current advances If deans and heads of departments in all medical schools were asked to coöperate, it should not be difficult to place every serving medical officer in a hospital clinic or university department for, say, twelve months every five years Everyone would gain from the transaction, the officers, though they have much to learn, have also something to teach and it would be valuable if the civilian and the Service doctor each gained first hand knowledge of how the other lived and thought If this arrangement became general the post graduate teaching of serving officers would be of two kinds the first, in their own colleges would deal with applications of medicine to military life the second in civilian institutions, would be devoted entirely to professional study and practice Collaboration in research and in training would bring life and reality to the liaison between civilian and Service doctors that was formerly maintained —somewhat shakily—through consultative and advisory committees

We express these thoughts at this time in the hope that something will be done not only to study the lessons taught by the war but also to sustain and develop the new vigour and opportunities that it has brought to British military medicine The Services should take the initiative now when their contacts with civil life are more numerous more close and more cordial than they have ever been before

Treatment of Osteomyelitis

THERE can be few diseases in whose treatment the sulphonamides and penicillin have wrought more welcome changes than in osteomyelitis Ten years ago it was not uncommon to see young adults with a recrudescence of infection, and a discharging sinus from the reopening of one of many scars, who gave a weary history of perhaps twenty operations Moreover a formidable mortality—up to 30% in some series—accompanied this distressing morbidity The rigid inelastic qualities of bone accounted for much of the trouble for such tissue is poorly adapted for the increased pressure of infection, is an easy prey to ischæmia, and even if the blood-supply was adequate to bring it could not accommodate a normal reactionary exudate with its powers for neutralising, immunising, and walling off Poor therefore in defence, bone is equally poor in recuperation, the dead bone takes long to separate and except in infants can seldom be absorbed but remains to provoke further sepsis unless removed Once bone destruction is well under way it would be futile to expect too striking a local improvement from chemotherapy, but much would seem possible with energetic treatment in the early stages; and by early we mean nothing less than the absolute beginning

Reports on the efficacy of sulphonamides in osteomyelitis show a restraint understandable when the frequency of the staphylococcus as the infective agent is considered (90%), and it is to penicillin that all eyes are turned ALTEMEIER and HELMSWORTH[1] record an impressive series of 34 cases treated with systemic penicillin with only one death, a grossly neglected case moribund on admission Where penicillin treatment was started within 3 or 4 days of the onset complete resolution was invariably obtained without any form of surgical intervention, the child appearing well in a week and often difficult to keep off his feet at the end of a fortnight Where delay had been longer, small soft-tissue abscesses requiring aspiration developed, but there was very little sequestration Even where delay had been excessive and bone destruction already certain, these workers maintain that the disease was quickly arrested, in most cases without surgery, and sequestration was minimal with some evidence of absorption and occasional spontaneous extrusion They note that where treatment has been delayed clinical improvement may not take place for some 48 hours or more after penicillin is started These results will not go uncontested, and DICKSON,[2] for instance, quotes two cases treated with penicillin and sulphonamides without drainage whose bone destruction continued, while another case given the same chemotherapy but drained by a small square window healed in 9 weeks ALTEMEIER and HELMSWORTH regard the X-ray changes customarily attributed to active destruction as indicating absorption of bone destroyed at an earlier stage of the disease They base this view on the fact that X-ray changes progress for 1–3 months after the cessation of penicillin treatment and after the patient is clinically cured This explanation may account for any apparently conflicting results of penicillin therapy

To attain good results, and perhaps settle the controversy immediate diagnosis followed by prompt action is an urgent clinical responsibility In laying down diagnostic criteria heavy emphasis must be laid on BRAILSFORD'S dictum,[3] that there is no X-ray diagnosis of osteomyelitis in the acute stage—10 days after onset is the earliest that radiological changes can be expected But the diagnosis should not be difficult to make on clinical grounds An acute pyrexial illness in a child or adolescent with pain in the region of a joint, a disinclination to move the limb, and tenderness localised to the end of a bone is sufficient to warrant penicillin therapy An infective arthritis or a simple cellulitis will cause the same symptoms but detailed examination is often sufficient to locate the site of the trouble, particularly in the early stages before too diffuse a reaction has occurred In cellulitis the swelling is asymmetrical, erythema early, and a cause commonly apparent Infective arthritis is uncommon as a "spontaneous" event, here the swelling is centred on the joint, effusion may be gross, and help may be obtained from the aspiration of turbid fluid DICKSON finds that the joint adjacent to infected bone is held slightly flexed and can usually be flexed a little more without pain but not extended No movement is free from pain if the joint is infected Osteomyelitis may, of course, lead to a purulent arthritis and will lead to a cellulitis, but since all these conditions will benefit from penicillin no case of possible osteomyelitis need await their differential diagnosis Acute rheumatism, on the other hand, is a little more worrying, for there is some evidence that penicillin may encourage rheumatic carditis[4], the evidence is not enough to preclude the use of penicillin in a doubtful case, but enough to make an accurate diagnosis desirable Rheumatism is characteristically flitting and the signs are referable to the joints rather than the bone metaphyses, the patient is fragile and hectic in appearance rather than severely toxic, delirium is almost unknown, and the leucocyte-count remains lower

The next question is how to prove that an early case which responds successfully would have been a full-blown osteomyelitis ALTEMEIER and HELMSWORTH find that minimal X-ray changes, in the shape of patchy rarefaction or slight periosteal reaction, commonly appear during or after recovery in even a slight case, although they discarded as incapable of proof three cases with no X-ray changes about whose clinical diagnosis they entertained no doubt. Since arrest of the disease at this stage is the desired goal, such cases may become more frequent and make assessment more difficult, but it is no new thing for penicillin results to lack a control, and in this disease it would be impossible to condemn any patients to provide one Moreover, unless blood-culture is positive the organism may not be isolated, though there is almost a hundred per cent chance of its being penicillin-sensitive We do, however, know something of the past and we can look to the future to provide results sufficiently different to leave no doubt Osteomyelitis in infants responds badly to operation and relatively well to conservative measures, in part owing to the fact that the streptococcus is the infecting organism in 40–50% of infant cases, and this organism causes far less destruction of tissues, bone or other

1 Altemeier W A Helmsworth J A Surg Gynec Obstet 1945, 81 138
2 Dickson F D J Amer med Ass 1945 127, 212
3 Brailsford, J S Proc R Soc Med 1945, 38, 555
4 Rantz L A, Spink W W, Coggeshall, H, Boisvert, P J Pediat 1945, 26, 576

than the staphylococcus. Streptococcal infection may also account for the group of cases distinguished by DICKSON in which an overwhelming septicæmia calls for conservative treatment

The accepted general measures in the treatment of these cases—rest, sedation, fluids, blood transfusion, &c—need not be discussed, because their use permits of no argument Where an obvious collection of pus has formed there is no excuse for departing from established surgical principles and drainage must be undertaken. It is possible that with early penicillin treatment this will rarely be needed It is certain that penicillin cannot be started too early

What are Bacteria?

THE full story of the bacterial cell cannot yet be told, but an interim report on existing knowledge should help the future historian and will stimulate the present generation to fresh research and new discovery Though it is nearing 300 years since LEEUWENHOEK described his little animalcules, progressive knowledge about bacteria began with PASTEUR'S demonstration of the intense and specific fermentative activities of these invisible creatures, which phylogenetically are most closely related to the blue green algæ KOCH and his pupils showed by original cultural methods the etiological relationship of certain bacteria to particular infections, but the next great step forward was made by PAUL EHRLICH, who introduced the theory of receptors on the bacterial cell to account for its specific affinities with dyes, antiseptics, and antibodies Modern chemistry and immunology have largely substantiated the receptor theory and have allowed big advances in the epidemiology and treatment of infectious disease DUBOS[1] has now marshalled a mass of information about bacteria in their relation to infection, with an understanding and profundity that excites the envy and admiration of the medical bacteriologist. First he describes bacterial cytology—the evidence for a nucleus as shown by the Feulgen stain rather than by ultraviolet or electron photography, the cell envelopes consisting of cytoplasmic membrane and rigid cell wall, the flagella of dubious origin uniting into a tail which acts both as rudder and propeller, the protective spore, and the defensive or aggressive viscous capsule The physicochemical behaviour of bacteria leads on to a discussion of their staining reactions, and particularly of the Gram stain which not only serves to differentiate bacteria but helps in an understanding of other bacterial properties, for the Gram reaction depends largely on the acidity or basicity of the cytoplasm

Immunochemistry has made great strides The chemical nature of many of the complex fractions of which the bacterial cell is composed has been determined, and a beginning has been made in using as immunising agents purified antigens such as the phospholipid (protein) polysaccharide compounds which constitute the O antigen of salmonella and dysentery bacilli Artificial antigens have been prepared which elicit the same specific antibody response as, for example, the intact pneumococcus Bacterial variation is another fascinating study whose relation to the natural history of infectious diseases and to the more general phenomena of life can only be guessed at Bacteria acquire new characters and enzymes, which remain as apparently permanent mutations, one pneumococcus type can be changed to another, and the activating substance, present in infinitesimal amount, has been identified as desoxyribonucleic acid Thus the bacteriologist has apparently accomplished a specific mutation by a specific agency, a feat which has so far defeated the geneticist

Virulence is a term borrowed from clinical medicine and used to define the capacity of a particular bacterium to produce disease But virulence is not a permanent intrinsic property of any bacterial species, it expresses only the ability of a particular strain of a given species, in a certain growth phase, to produce a pathological state in a particular host when introduced into that host under well-defined conditions In other words, virulence is a term applicable to the host parasite relationship rather than to some unique attribute in the bacterial cell However, some bacterial properties which enable the parasite to establish itself and produce disease in the host are now known For example, gram negative bacilli in the smooth phase (i e, possessing the complex protein polysaccharide antigen), encapsulated bacteria like the pneumococcus, and streptococci with the protein M antigen, are able to withstand the host's defensive mechanism, whereas bacterial variants deprived of these characters are usually avirulent The possession of these specific substances allows the bacterium to resist phagocytosis, apparently by neutralising complement or natural opsonin Again the invasiveness of bacteria may depend on their ability to withstand higher temperatures, to grow in particular gaseous environments, or to utilise certain nutrient substances, besides the faculty of producing destructive toxins, lysins, or enzymes There is a large field for study here, the elective affinity of bacteria for different tissues, the variation in invasiveness of different bacterial types (e g, among the pneumococci and the salmonellas) within a particular species, the chemical nature and pharmacology of toxins and enzymes, and the function of the spreading factor are matters about which little is yet known The new knowledge about the bacterial components and their relation to virulence has been followed by the preparation of better but also more specifically limited immunising vaccines, and DUBOS pleads for more research into the value of non specific antigens—e g, of rough pneumococci or group A streptococci—which may result in a broad resistance to infection to all the individual types of the species A rational approach to chemotherapy has been made possible by an understanding of the essential metabolites of bacteria, and FILDES'S hypothesis of the bacteriostatic or bactericidal action of sulphonamides and other substances has with modifications, been generally accepted

Thus study of the physiology and immunochemistry of the bacterial cell has had far reaching results in the understanding and control of infection. But much is yet to learn, and the research student will find this book by DUBOS a useful base from which to launch new attacks

[1] The Bacterial Cell By R J Dubos professor of comparative pathology and professor of tropical medicine at Harvard University London Oxford University Press 1945. Pp 469 25s

Annotations

LURE OF THE ALPS

THE upland valley of Davos came to our knowledge as a winter resort when John Addington Symonds, visiting T H Green the philosopher on his way to Egypt in the late summer of 1877, found the climate suited him so well that he decided to winter there, and soon made it his home, building a chalet called *am Hof* R L Stevenson, with his wife and his stepson, Lloyd Osbourne, joined the Symonds two years later at *am Stein*, conveniently situated at the top of the famous Buol toboggan run which led past *am Hof* Mrs Oliphant came to live at the Hotel Victoria, Beatrice Harraden at the Curhaus, and the scene was set for the best publicised resort of poitrinaires in the world And justly too, for among the few flat-bottomed valleys in Europe 5000 feet or more above sea level Davos is unique in having the sunshine and the prevailing wind coming from opposite points of the compass New hotels and pensions met the influx of visitors, villas sprang up in the "English quarter" between Platz and Dorf, and the wise and genial Huggard guided the regime of the invalids before the era of strict sanatorium discipline set in "You may skate, but must not tumble" has been handed down as his attitude to winter sport. It was a life of vivid contrasts—hot sun and sharp frost, perilous gaiety and patient convalescence, comforting friendships and bitter nostalgia—with the prospect of recovery far brighter for the well-to-do The Invalids' Home was a praiseworthy but disappointing effort for the less well-off, and a happier day dawned when, just before the first world war, an English sanatorium was built with money raised by the sixth Lord Balfour of Burleigh Obliged to close during that war it was not reopened, partly owing to economic depression and partly to the wave of doubt about the net value of alpine treatment which made even a Douglas Powell hesitate to send patients to Davos. The sanatorium was sold to the last Swiss canton that lacked one, and the money was invested to "help tuberculous patients of small means to obtain treatment in Switzerland" During the inter-war period this help was given with a modest success, brightened by an altogether satisfying episode when youngsters from the Birmingham Children's Hospital were given the chance of a prolonged stay in the Alps to clear up asthma or bronchiectasis And now after a second war-time interruption, during which the Queen Alexandra Sanatorium Fund has accumulated, the council has decided to use it strictly for the convalescence of patients who have completed their more active treatment in British sanatoria They are to be selected by the hon examining physicians in London from those who have made such progress that they no longer require close medical observation or nursing Preference will be given to those certified by sanatorium chiefs to be fitted, both physically and temperamentally, to complete their recovery in the freer atmosphere of an open health resort. We believe this decision is a wise one and that so used the fund will give its maximum output in health and happiness

EDUCATION FIRST

CHILDREN should certainly learn something of the structure and behaviour of their body, but they should never be taught to take all its complaints seriously. Dr John Cahill, in an address to the Middlesbrough Head Teachers' Association,[1] has lately made this distinction afresh Education, he considers, is more important than health, for unless we are fit to live our lives and do our work there is little point in being fit; and the work of the child is learning He finds most of us much too fussy about our health, and has little enthusiasm for minor-ailment clinics for school-children. If these clinics were conducted outside school hours, he says, they would always be as deserted as they are during the holidays As it is, the idle young are charmed to gather for the treatment of small cuts and scratches which they ought to be taught to ignore He quotes the sturdy dictum of John Locke

> "In the little harm they suffer from knocks and falls they should not be pitied for falling, but bid to do so again which besides that it stops their crying is a better way to cure their heedlessness"

True · but it will hardly prevent tetanus in the one unlucky child The doctor, in fact, is nowadays often in a dilemma should he risk doing mental harm to a child by treating him unnecessarily, or should he risk doing him physical harm by neglecting a seemingly trifling lesion? Dr. Cahill's answer is that we must at least avoid excessive zeal in treating him "sympathy is a dangerous drug and should be saved for those who deserve it" Quoting the late Sir John Collie's advice that a man who has been ill should resume work before he feels 100% fit, Cahill applies the principle to school-children He believes that by improving their diet you may improve their nutrition and their health and strength, but he distrusts all claims that better nutrition improves intelligence, scholastic performance, or morals Nor is he impressed by public nurseries and nursery schools, teachers in Middlesbrough, he said, find it is the nursery child, and not the child straight from home, who has difficulty in adapting himself to the routine of the infant school The best Cahill could say was that a public nursery is better than a bad home

Environment, though it may have little effect on physique, plays a large part in shaping thought, habits, and manner, and he believes that the psychological field offers our most promising line of advance for the future He quotes Clark-Kennedy's view[2] that "a certain amount of stress, strain, and risk is necessary for the maximum development of human character" Most people living in the past thirty years have had ample opportunity to profit from the benefit of all three, and many will feel that Dr Cahill is making a reasonable request when he invites us to "plan as men who hope only for small steps forward and not as dreamers do" All the same, those who don't ask don't get

NEW TEST FOR TRICHINIASIS

THE diagnosis of trichiniasis remains largely a clinical problem—the acute abdominal symptoms, followed by fever, muscle pains, eosinophilia, and œdema of the eyelids are fairly characteristic, and if the history of eating undercooked sausages or pork a few days previously can be elicited the picture is complete. Unfortunately in most patients some of these features are missing, and the physician then naturally asks for laboratory tests to confirm his tentative diagnosis

Two years ago the position of laboratory tests in diagnosis was discussed in these columns,[3] and the conclusion reached was that while improvements in the antigen, such as the preparation of a pure specific polysaccharide, might prove helpful in the diagnosis of acute infections, no serological method is likely to enable old infections to be detected with anything approaching certainty Roth,[4] in Sweden, has lately published a method for the serodiagnosis of trichiniasis using living trichinella larvæ He confirms the previous findings that skin tests with a trichinella extract have their value, but they may fail to give a positive reaction in mild cases and sometimes give nonspecific reactions. His method, which he has been using since 1941,[5] consists

1 *Med Officer*, Sept 15, p 87

2 Clark-Kennedy, A E The Art of Medicine in Relation to the Progress of Thought London, 1945

3 Leading article, 1943, II 295

4 Roth H *Nature, Lond* 1945 155 758

5 *Acta path microbiol scand* 1941, 18, 160

of incubating living trichinella larvæ (obtained by artificial digestion of their cysts) with sterile serum from the suspected patient at 37° C on a hollow ground slide with a coverslip in a glass dish containing moist filter paper to avoid desiccation In positive sera after five hours the larvæ are still very motile, but finely granular precipitates are found near the anterior end of a large number of the worms After twenty four hours the larvæ are shrunken and the precipitates are found lying free in the serum The amount and form of the precipitate varies much with the age and intensity of the infection the reaction usually becomes positive between 10 and 20 days from the first symptoms of the disease; in mild cases the antibodies seem to disappear again in about a year Roth claims the test "often to be more sensitive and more specific than the usual intradermal and precipitin tests with trichina antigen" Unfortunately he gives no data by which this claim can be assessed, and it remains to be seen whether it is substantiated by further experience

The test seems unlikely to be of practical use in any country where trichiniasis is rare since the supply of live trichinella larvæ is likely to be lacking at the time they are needed, but it is interesting as a new line of approach Physicians will have to continue to rely chiefly on their clinical judgment, aided by skin tests if any antigen is available It is worth emphasising here again what Beeson[6] said in 1941—that a change in an acute illness from a negative to a positive reaction, or a rapid rise in the eosinophil count is diagnostically much more significant than any single positive skin test or single eosinophil determination

THE PHILOSOPHY OF JESUS

"after two thousand years there are more people familiar with, interested in, and influenced by, the career and record of Jesus than there are in the sayings and doings of any other figure in history real or mythical"

Dr Harry Roberts and Lord Horder in their new book[7] are not concerned with the divinity of Jesus; for them he was the son of man, like the rest of us and like the rest of us the son of God His philosophy, as they see it is a way of life in which the claims of the individual are always honoured, and it is in this sense that they interpret his teaching of the "great heritage of hope" Though this teaching derives from the Jewish scriptures, he purged it (in F H Stead's words) of "the narrow nationalism which exalted the Jew above the rest of mankind, and of the petty localism which made Zion the seat of universal sway and worship, but he retained and sublimed its notes of pardon equity, kindness peace, plenty and health" He offered no dogmas or disciplines being content to teach the broad principles of tolerance and mutual respect In an age which disparaged them, he found women as worthy of attention as their husbands and brothers and no less capable of rational conversation and spiritual insight His teaching the writers of the book feel, was positive where that of Buddha was negative Buddha taught men to renounce the world and achieve the calm which comes from the annihilation of desire For Jesus, on the other hand salvation for oneself alone meant nothing he shared fully the lives of those about him; he told his tales in their everyday idiom, he wished them not to evade the world but to live well in it In this Dr Roberts and Lord Horder see the basis of democracy, which is "the control by individuals or groups of those things which specially concern them founded on the theory which all experience goes to verify that in the long run no one will look after a man's true interests so well as himself"

Jesus set no higher standard of social conduct than that men should love their neighbours as themselves, which is the very antithesis of the mastery of one man by another Anyone who has understood and accepted the Christian doctrine of equality is perforce a democrat Jesus took the line that no civilisation can advance beyond the intelligence, the strength, and the morale of the bulk of the common people considered as individuals His reforms were planned to spread from the individual to the general To the attainment of this end the form of his teaching was perfectly suited

PENICILLIN AND BLOOD-COAGULATION

Among the remarkable properties of penicillin its lack of toxicity to higher animals stands only second to its powerful action against some single cell organisms it is doubtful whether any other biologically active substance has so little unwanted pharmacological effect in the mammal Van Dyke[1] could produce only small and reversible effects in mice by giving enormous doses of crystalline penicillin The minor signs of toxicity which occur in man have usually been attributed to impurities, *though crystalline penicillin can produce skin reactions*[2] One of the most troublesome reactions before intramuscular administration came into favour was thrombosis in veins used for injections or infusions of penicillin, and there was a general assumption that something in the material injected—possibly one of the impurities—favoured thrombus formation either directly or by damaging the vessel wall No other reaction which could be attributed to thrombosis seems to have been reported; and it is worth noting that in the first substantial series of cases of subacute bacterial endocarditis treated with penicillin and heparin[3] the results were very much like those in later series treated with penicillin *alone*

Though intravascular thrombosis and the clotting of shed blood cannot be compared directly, these facts are recalled by the recent report[4] of a pronounced effect on the blood brought about by penicillin given in doses of a size which is now fashionable in therapeutics—200,000 units by mouth in enteric capsules or 50 000 units intramuscularly In blood samples from a group of 20 patients the fall in coagulation time was roughly proportional to the rise in penicillin content Penicillin administration was also followed by a fall in bleeding time and a change in the character of the clot which became non retractile and like an artificially produced solid thrombus The values for coagulation time throughout the experiments quoted scarcely fall below normal limits, so far as can be discerned from the details given Estimations of coagulation time are notoriously liable to fallacy and require repeated confirmation and the American workers do not discuss the curious finding that coagulation time and bleeding time which depend on unrelated mechanisms, were both affected The report, which is a preliminary one gives no indication of the variations found between different patients (there is great quantitative variation in the way the body deals with penicillin) and in only one out of three curves is the blood level of penicillin shown More details also of the purity and of the brand or brands of penicillin used are wanted, since there is at present no evidence whether penicillin itself or one of the substances which constitute the impurities in commercial preparations was responsible for the effects described It seems remarkable if the rapid clotting and non retractile clot have been overlooked by the hundreds of workers who *have taken blood and prepared samples of serum from* patients receiving penicillin, unless indeed the size of the dose was concerned, since the intramuscular dose

6 Beeson, P B. *Lancet*, 1941 II, 67
7 The Philosophy of Jesus Harry Roberts and Lord Horder Dent London 1945 Pp 131 2s

1 van Dyke H B. *Proc Soc exp Biol*, N Y 1944 54 218
2 Welch H Rosenberg A., jun. *J Amer med Ass* 1944 126 10
3 Loewe L Rosenblatt I, Greene H J., Rosell M *Ibid* 1944 124 144
4 Moldavsky L F., Hasselbrock W H., Catano C Goodwin D *Science* 1945 102 35

given in these experiments was 3 times as large as that known to be satisfactory for most infections, and hitherto usually used. The one curve given for the content of penicillin in the blood did not reach a higher level than that often found after smaller doses, but it is possible that less readily excreted impurities reach a higher concentration in the blood after the larger dose, so that the effect becomes manifest After encountering severe hæmorrhages in two cases of bacterial endocarditis treated with penicillin, one of which received heparin as well, Hines and Kessler [5] have investigated the effect of penicillin—this time in the ordinary dose of 10,000 units intramuscularly—on various blood constituents and on the prothrombin-time and heparin tolerance in 10 patients with various diseases. There was no effect except on the heparin tolerance, which is tested by injecting 10 mg of heparin intravenously and thereafter examining the blood at intervals of a few minutes for changes in coagulation-time. Usually there is a slight increase in patients receiving penicillin, and drugs such as digitalis and the salicylates may also change the tolerance In 2 of the 10 patients receiving penicillin there was an increase in heparin tolerance well beyond the usual limits (to 7 and 13 5 minutes by the capillary-tube method) accompanied by alarming reactions resembling the symptoms of allergy. Possibly penicillin or one of its impurities affects at some point that physical disturbance of a "constantly operating dynamic equilibrium," of which Macfarlane [6] suggests that clotting is the result

THE PART AND THE WHOLE

In his account of the medical state of New Zealand industry (see p 537), Dr J. M Davidson points out that in the British Factories Act of 1937 "bodily injury" is held to embrace "injury to health" Logically, as he says, this position should be reversed, for "injury to health," which covers any departure from physical or mental fitness, is a more comprehensive term than "bodily injury," which is generally taken to mean the result of some trauma or toxic process There is more in this than hair-splitting, for if legislation places the emphasis on injury rather than health, administrative practice will develop accordingly. This is what has happened in our own country, where the factory inspectorate has been concerned primarily with the prevention of accidents (traumatic or toxic) and has assigned a secondary place to other aspects of industrial health The question of emphasis on "bodily injury" or "injury to health" raises in fact, two practical issues: (1) whether control of industrial health administration should rest with the layman or with the doctor, and (2) which department of Government can best take care of the health, safety, and welfare of the industrial worker

As a correspondent has remarked,[7] we are liable to be bluffed by words and to assume that because a Ministry is called "Labour" it is the natural place for the administration of all matters connected with factories Equally, the fact that a Ministry is labelled "Health" does not necessarily mean that it is the best department to administer all health affairs, especially when its experience is limited to a few branches of medical activity. If, however, the medical services of this country are to be integrated, there does seem to be a strong case for arranging that industrial health should be the concern of the department responsible for the other principal health services The arguments that led to the exclusion of industrial medicine from the white paper on a National Health Service have never carried much conviction

5 Hines L E, Kessler, D. L. *J Amer. med Ass* 1945, 128, 791
6 Macfarlane, R G *Proc. R Soc Med* 1945, 38, 399
7 *Lancet* 1945 i, 225

END OF A CONTEMPORARY

Doctors in the Forces mostly work in small groups or by themselves Especially in war-time, with its inevitable influx of individualist civilians, it is no easy matter to ensure that each medical officer shall feel that he is part of a great service to which, whether he is busy or perforce inactive, he is making a valuable and valued contribution It will help him to carry out his duties confidently if he is in some kind of direct touch with the men in charge of the service, and comes to think of them as colleagues who, though they may hold high rank and speak in administrative orders, are yet concerned with gaining for the troops the utmost advantage from medical science

The *Army Medical Department Bulletin*, which has just issued its 51st and last number, was one of the means whereby the War Office sought "to keep alive and keen a sense of professional unity and interest among Army medical officers" Started in 1941, the bulletin had at first a faint flavour of ACI, and it can seldom have been easy to present controversial topics informally to the satisfaction of all the many administrators and consultants who might veto publication. Nevertheless to the credit of all concerned, including the administrators and consultants, much interesting material was cast in readable form; and in the past two years the *AMD Bulletin*, with its supplements, distributed to officers of the RAMC and also of the EMS and other Services, has been an example of medical journalism in the best British tradition—sound, practical, unpretentious, and written in a friendly tone which must have made many a recipient feel that human hearts beat even in Hyde Park Gate It was also in the British tradition that this essay in group psychiatry and postgraduate clinical training was entrusted (it is said) to pathologists Whether it is wholly desirable that pathologists should assume all the key positions in professional life is no doubt an open question, but we are naturally biased in favour of a contemporary which goes out of action with the words: "Now that the war is over and medical journals will again become fully available, we commend a regular study of their leaders and annotations to readers who may regret our departure"

We have to announce the death on Oct. 21 of Mr D C Rayner, emeritus professor of obstetrics in the University of Bristol, at the age of 80.

The War Office has announced the following dates for release in the United Kingdom of men and women medical and dental officers Group 21, Nov. 12 to 24; Group 22, Nov 25 to Dec. 6, Group 23, Dec 7 to 20

The University of Birmingham proposes to appoint full-time professors of medicine, surgery, gynæcology, and pædiatrics, each at £2500 a year. If suitable appointments can be made, the new chairs will be inaugurated next March The professor of pædiatrics will have charge of the institute of child health The cost of the salaries will be largely met from the Treasury grants to medical schools announced by the late Government

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In the six years just behind us the health of children in this country has in general not suffered Lord Woolton, giving his presidential address to the Central Council for Health Education (*Times*, Oct 20, p 8), found in this great cause for satisfaction Indeed, many children, he said, are better nourished than they would have been before the war We have learned much about keeping them fit, and especially about the value of milk, orange juice, and cod-liver oil, not only to children but to nursing mothers. These three foods, he considers, must become part of our national system of preventive medicine; and he reminded the meeting of our debt to the United States for supplies of orange juice during the war—supplies which he hoped would continue. He is anxious that children should learn more about sound bodies and the rules and habits of good health, and would like to see health education, physical training, and some training in food values made a part of the school curriculum.

Reconstruction

THE LONDON BOROUGHS

THE white-paper on a National Health Service proposed that the county of London should be a single unit for the purposes of the service Commenting on this proposal last December the London County Council suggested that they should be made the authority for planning, controlling, and administering the service throughout the county, but should delegate to the *metropolitan borough councils*

(1) The maternity and child welfare work at present undertaken by the borough councils, excluding the comparatively small amount of institutional work they now do, which should be undertaken by the LCC
(2) Administration of tuberculosis dispensaries, provided they are properly linked with the hospitals sanatoria, and consultant services.
(3) Epidemiological inquiries, subject to a closer link with the LCC's laboratory services and fever hospitals

On Tuesday, the *general purposes committee* presented to the Council some conclusions on these subjects, reached in agreement with representatives of the Metropolitan Boroughs Standing Joint Committee

Maternity and Child Welfare—Under (1) the expression "institutional work" is defined as the provision, directly or indirectly, by a maternity and child welfare authority, of residential accommodation for expectant or nursing mothers and for children who have not attained the age of five years and are not being educated in schools recognised by the Ministry of Education" The LCC, it is thought, should make central arrangements for the pooling of beds, which so far as practicable, should be allotted in particular institutions to particular boroughs and should also negotiate the terms on which such beds should be provided in voluntary establishments

Tuberculosis dispensaries, in the committee's view, should be in or near a general hospital at which consultant services of all types are available (including radiography, pathological investigations, and artificial pneumothorax treatment), but should retain their separate identity This principle should be observed in establishing any new dispensaries, but it may, of course, be many years before many existing dispensaries can be moved to more suitable sites. If possible, each medical teaching centre should be linked to a tuberculosis dispensary

Tuberculosis officers—The report also discusses the status, qualifications, and duties of tuberculosis officers.

Hitherto tuberculosis work has been sectionalised One individual, the metropolitan borough council's tuberculosis officer, has been in effect responsible for outpatient work at the tuberculosis dispensary; another the Council's hospital superintendent, for inpatient work in hospital; and a third, the Council's sanatorium superintendent, for another type of institutional work. In addition, the metropolitan borough council's tuberculosis officer has been nominally an expert in all types of tuberculosis, including that of the bones and joints, glands skin, &c.

'We are advised that the whole modern tendency is for the tuberculosis officer to become primarily a chest physician, expert in all kinds of pulmonary conditions and responsible not only for the outpatient care of the patient but also in charge of beds The tuberculosis service should be regarded as a career in itself and not as at present, as a stepping-stone to other positions e.g., that of borough medical officer of health A tuberculosis officer should in fact enjoy the status of a consulting physician, and the ultimate aim should be that he should have charge of beds in tuberculosis wards and act as chest consultant for patients in general wards of a hospital'

It is recommended that each tuberculosis officer should visit one of the Council's hospitals regularly, and when circumstances permit become responsible for the diagnosis and treatment of chest cases there In return for such part time service the LCC would contribute to his salary (paid by the borough), and candidates for a dual appointment of this kind would be selected jointly by the LCC and the borough

It would be an advantage if every three years or so the tuberculosis officer could spend up to three months in postgraduate study at a sanatorium or in travel The report suggests that while he is away, a medical officer of the Council should replace him, if so desired.

Infectious diseases—As regards laboratory services the committee thinks that the various arrangements made by the boroughs (including arrangements with voluntary and municipal hospitals and with commercial organisations) are generally satisfactory, and it recommends no alteration. If, however, the Government establish the contemplated National Public Health Laboratory Service, reconsideration will be needed

"Arrangements are nearing completion whereby a consultant may be called in from one of the Council's fever hospitals by a metropolitan borough council to advise in difficult cases of diagnosis of infectious disease"

Default.—Proposals are made about the steps to be taken when the LCC is dissatisfied with the way in which a borough is carrying out its delegated duties

Special Articles

INDUSTRIAL HYGIENE IN NEW ZEALAND

It has often been said that in social legislation New Zealand leads the world, in fact to the average Englishman it is a utopia—a perfect country For this reason Dr J M Davidson's report[1] on the state of industrial hygiene there will cause some surprise

As one of HM medical inspectors of factories, Dr Davidson was lent to the New Zealand government in 1944 to survey conditions of work in the factories of the Dominion Visiting over 200 factories in town and country he was struck by the diversity of trades, though (as he points out) New Zealand is not yet a highly industrialised country Heavy industries such as steel making have not yet been established The primary industries such as milk, butter, and cheese production have been largely transformed by modern methods of mechanisation until the conditions obtaining in them differ little from those in the secondary industries Most of the industrial processes are carried on in small factories which need relatively more State supervision if the health of the workers is to be safeguarded Merely to keep a factory clean costs money, and the small firm has less to spare for what are too often regarded as unremunerative "frills"

ROOM FOR IMPROVEMENT

Inevitably comparisons and contrasts are made between conditions of work and factory legislation in Great Britain and New Zealand. Most of the New Zealand legislation quoted is from the Factories Act of 1921–22 as amended by the Factories Amendment Act 1936 which deals mainly with hours and wages. The corresponding British Factories Act is dated 1937 It should be borne in mind, however, that the British Act of 1937 emerged only after long years of discussion and was long overdue, the previous Act being passed in 1901 Today New Zealand is in much the same position as Great Britain was before 1937 because it is trying to "make do" with an Act which is largely out of date The legal position is complicated also by various awards made by the Court of Arbitration, many of them laying down conditions of work in the factories

Perhaps the most surprising feature of New Zealand factory law is that when Dr Davidson went to the Dominion, it was still possible "for a child of 13 to be legally employed in a factory under very poor conditions for periods up to 11 hours per day (excluding meal times) and for 56 hours a week.' In some cases children of 12 years of age could be seen working in factories. In a footnote to the report it is stated that an amending Act now prohibits the employment in a factory at any time of a boy or girl under 14

In a sunny open-air country like New Zealand it is strange to read of the low standards of natural lighting, general ventilation sanitary accommodation and cleanliness of factory buildings. The legislation on these points is weak and compares unfavourably with the standards laid down in Great Britain Washing facilities for the workers in New Zealand factories are scanty or wholly absent" Even in food factories it is unusual to find really good, or even adequate washing accommodation

1 Appendix to the Annual Report of the Director-General of Health New Zealand, 1945

In some factories trained nurses have been appointed to well-equipped ambulance rooms, and in a smaller number part-time medical officers attend regularly to examine, advise, and treat the workpeople Dr Davidson remarks that "here we have the nucleus of a medical service in industry" But he goes on to say that it is not sufficiently recognised that there is a greater need in industry for a health service than for a (curative) medical service The system of social security in New Zealand aims at providing outside the factory whatever form of treatment a person may need, but it makes no ad-hoc provision for the supervision of the industrial worker at work Where a doctor has been appointed to a factory his work is mainly curative and not preventive

Responsibility for accident prevention in factories is divided between the Department of Labour and the Marine Department—a fact which Dr Davidson regards as unfortunate because in his opinion such division of responsibility makes for inefficiency Neither the inspectors of factories nor the inspectors of machinery of the Marine Department have had training in safety engineering, and indeed the inspectors of factories often investigate only the wages and compensation aspects of the accidents

RECOMMENDATIONS

Dr Davidson thinks that an effort should be made to raise the general hygienic and æsthetic standards in factories throughout New Zealand, to provide greater safety from accidents, and to improve in particular the conditions under which young persons are employed

More care should be taken by employers in planning new factories with an eye to the type of work to be done Medical and nursing supervision should be provided, and a higher standard of first aid should be established Boys and girls should receive special training at work, especially before being put on to dangerous machines Industry should appoint its own safety officers to deal with accident prevention

Regarding the responsibility of the State it is recommended that the existing legislation should be codified and simplified The employment of children under 14 years of age in factories should be prohibited (as has since been done) and all persons under 16 should be medically examined before being employed

More should be done to educate factory managements and workers in hygiene Also, higher standards of factory inspection are needed, and to this end the system of recruitment of factory inspectors should be improved along specified lines They should be trained by experts in industrial health and hygiene, toxicology, psychology, sociology, and accident prevention The inspectors, when suitably trained, should be made responsible for all routine work in connexion with the guarding of machinery, but should be guided in such matters by the inspectors of machinery They should be relieved of all duties involving consideration of monetary aspects of employment and compensation for injury

As regards administration Dr Davidson suggests the formation within the Department of Health of a division of industrial hygiene which would take over from the Department of Labour responsibility for the care of the industrial worker at work in so far as his health, safety, and welfare—but not remuneration—are concerned The reformed factory inspectorate should be attached to this division In expanding this recommendation he says that the purpose of a factory inspectorate is to ensure the health, welfare, and safety of the factory worker Bodily injury is a special form of injury to health, and accident prevention is only part of the general problem of the maintenance of health All matters affecting the health of the worker should be dealt with by one department, the Department of Health "Dual control leads to dereliction of duty, and the present cleavage of responsibility whereby the Department of Health has control of the environmental health services outside the factory and the Department of Labour controls those inside should be abolished"

A possible criticism of Dr Davidson's report is that it gives the impression that factory conditions in this country are nearing perfection On closer reading, however it will be found that his main theme is that factory legislation of Great Britain is more advanced than that of New Zealand It may comfort our cousins in the Dominion to know that here we still live in glass houses and sometimes in no houses at all

ROYAL COLLEGE OF PHYSICIANS

SPEECHES AT THE HARVEIAN DINNER

LORD MORAN presided over an impressive assembly at the Dorchester Hotel on Oct 18 when the Royal College of Physicians of London held their first Harveian commemoration dinner since 1938 The PRIME MINISTER proposing the toast of The College, said that in these times of change we should do well to consider the continuity of effort which it represented The last of its 420 years had been spent under the shadow of sudden death, but in war man's inventive genius was stimulated towards preservation as well as destruction and made advances in the art of healing. One advance which would have been of special interest to Harvey was the development of blood-transfusion services On a visit to a hospital in Normandy soon after D-day Mr Attlee had been amazed how well the men looked apart from their wounds, compared with the pale faces he remembered in the war of 1914–18. He paid tribute to the doctors who had served in the Forces and to those who had borne an ever-increasing burden of civilian practice as the younger men were drawn away to the war

Turning to the future and to plans for the health services, Mr. Attlee said that, whatever the difficulties of arriving at an agreement on means, he believed that the ends pursued by the Government were approved by the whole country They were seeking a service available to every member of the population and covering every form of medical activity. But the service should be one in which professional men and women were able to devote themselves to their great calling without financial anxiety and without feeling cramped and over controlled by regulations We needed a great improvement in our hospital services, in facilities for diagnosis and treatment outside hospitals, in the number and distribution of consultants and general practitioners and perhaps above all in the planning and organisation of the different branches of medicine into what must be an integrated whole—a real National Health Service The Government realised that for this to be successful they must have the help and coöperation of the profession, and they knew the profession was as eager as the Government to see that the service was really good He gave the toast of The College in confidence that this help and coöperation would be given as unstintingly as in the past to the great causes which challenge us

Lord MORAN in his reply recalled how the college as long ago as 1637 had recommended to the Government "the provision of a commission or office of health"—advice which was acted upon three hundred years later when the Ministry of Health was established The college was not discouraged, it still made suggestions hopefully, and he thought of late the tempo had quickened a little Comparing the qualities which make for success in medicine and politics, he quoted Burke's dictum that no small part of a statesman's task is to know what to avoid Certainly the best physician was the one who committed the fewest errors in diagnosis, and the physician who never forgot the distinction between what he knows and what he only thinks he knows would not go far wrong Success, however, could be won in both professions by the gift of the gab, and the greatest danger to the doctor's integrity of mind was the credulity of his patients If the credulity of the public was a snare to both professions, the only remedy was the education of public opinion, and to rouse public opinion he held, we must make it clear that moral issues were involved and appeal to the best in men

Medicine and politics had much in common, but would they go forward into the future in step? Medicine was becoming more scientific, and Lord Moran warned the politician that he must not deride science as high-brow stuff; for, if he did, science would rub his nose in the facts It sometimes seemed as though the indifference and want of sympathy shown towards the scientific point of view by so many of our countrymen was the greatest menace to our prosperity In this war we had been saved from utter ruin by our children If we remembered what they had done for us, surely we would go forward into the future without bitterness and faction, working together as one people for the betterment of all mankind

Dr JOHN PARKINSON, who earlier in the day had delivered the Harveian oration on rheumatic fever and heart disease, proposed the toast of The Guests; to which the ARCHBISHOP of CANTERBURY replied with some assurance, for (as he pointed out) he had to do the same work as most of them—and more also The Prime Minister, for instance, merely controlled a cabinet of his own choosing, but the Archbishop had to control a bench of bishops chosen by the Prime Minister Again, though the Lord Chancellor administered the law, everyone knew what the law was; whereas neither the Archbishop nor anyone else knew what the ecclesiastical law was The Secretaries of State for Foreign Affairs, the Dominions, and the Colonies all had the backing of vast Government departments; whereas with the help of only two chaplains one secretary, and one typist the Archbishop did their jobs too, and in his afternoon coped with the affairs of Tanganyika, Czechoslovakia the Russian Orthodox Church, and the Patriarch of Yugoslavia Moreover unlike the Lord Mayor of London, who had only to keep his end up for a year, or Mr Eden who had periods of relief as a displaced person, the Archbishop had to go on for ever

Mr ERNEST BEVIN, the Foreign Secretary, who also spoke for the guests, thanked the college for the help they had given him, in his previous office, in the field of industrial medicine, but admitted he was still unsatisfied and impatient Five thousand years ago Moses had insisted on one day's rest in seven, and despite modern scientific developments we had not got a second yet, though mechanised methods had doubled the demand made on the worker in his six days of labour Men were weary, and he sometimes wondered if the managerial classes fully appreciated the physical effect of this fatigue on the masses For many years we would be desperately short of effective man power, for we were now feeling the gap in the 45–55 age group caused by the last war and the loss of training caused by this one We could not afford to lose the life of a single child, and he appealed to the medical profession to throw aside prejudice and put their ability at the service of the community ' so that this grand old race may survive and still play its part in the destiny of human affairs."

The guests included—

Viscount ADDISON, Secretary of State for Dominion Affairs; Mr A V ALEXANDER, First Lord of the Admiralty; Sir FRANK ALEXANDER, Lord Mayor of London; Mr ANEURIN BEVAN Minister of Health; Sir EDWARD BRIDGES; Admiral of the Fleet Lord CUNNINGHAM, Dr H GUY DAIN, chairman of council BMA Sir WILLIAM DOUGLAS, secretary, Ministry of Health Sir HERBERT FASON, president of the General Medical Council; Mr ANTHONY EDEN; Sir WILLIAM GOODENOUGH; M FEODOR GOUSEV, the Soviet Ambassador; Mr G H HALL, Secretary of State for the Colonies; Mr FARDLEY HOLLAND PRCOG; Lord JOWITT Lord Chancellor; Mr W L. MACKENZIE KING, Prime Minister of Canada Mr WELLINGTON KOO the Chinese Ambassador; Prof S A KROGH; Sir ALAN LASCELLES; Lord LATHAM; Lord LEATHERS; Mr OLIVER LYTTELTON; Mr DESMOND MACCARTHY; Lord McGOWAN M RENÉ MASSIGLI the French Ambassador Prof D HUGHES PARRY vice-chancellor of the University of London Marshal of the Royal Air Force Lord PORTAL; Sir ARTHUR RUCKER, deputy secretary Ministry of Health Mr H B SOUTTAR, president of the BMA; Sir ALFRED WEBB-JOHNSON, PRCS; and the presidents of many other medical bodies

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MEDICAL SOCIETY OF THE LCC SERVICE.—A meeting devoted to pathology will be held at Archway Histological and Group Laboratory, Archway Road, Highgate, N19, on Wednesday, Nov 7, at 3 PM

SOCIETY FOR RELIEF OF WIDOWS AND ORPHANS OF MEDICAL MEN—At a meeting of the court of directors on Oct 10 with Dr R A Young the president in the chair it was stated that in the half year ended June 30 the sum of £2002 10s had been given in relief to 55 widows; £251 had been received in subscriptions and donations, and the expenses were £198 Relief is granted only to the necessitous widows and orphans of deceased members Membership is open to any registered medical man who at the time of his election lives within 20 miles of Charing Cross Particulars may be had from the secretary at 11 Chandos Street Cavendish Square London W1

In England Now

A Running Commentary by Peripatetic Correspondents

"CAN a rose become a bud again?" One hesitates to compare hoary headed doctors with buds or even roses, but if we could the simile would be apt for those of us who are taking postgraduate exams For visions of Queen Square come before us and for a few hours we think the thoughts of youth again

The kindly examining board had decided that instead of travelling some two hundred miles up to Town I could write my paper at a nearby West of England city On arriving punctually at 1 45 at the hospital indicated on my card I appeared to be expected by no-one I wandered what seemed endless miles along hospital corridors, and finally landed up in what appeared to be the nurses' sitting room Was I sitting for the second year nurses exam, they inquired? My reply that I could not possibly rise to that, but that I was hoping to write a paper for a diploma of one of the Royal Colleges was received in silence, their expressions showing that they obviously thought that even their *first* year exam would be above my standard Things were at a standstill till finally one nurse, brighter than the rest, remarked that she had seen the porter dusting the chairs in the Board Room that morning so something must be going to happen there So to the Board Room I went, where I found some more candidates, and a cheerful secretary who, having provided us with the question paper and wished us good luck, departed, promising us each a cup of tea during the afternoon

Then it was that the clock went back and I was transported again to Queen Square the only difference being that the monotonous tramp of luckless candidates being conducted to and from the cloakrooms was absent, and instead of sitting at hard desks sucking sweets with the vain hope of stimulating our brains to action we sat round a large table smoking and drinking tea as we wrote However the three hours soon went and again I was back in 1945 wondering whether Mrs Smith with the suspected placenta praevia had really gone into labour during my absence, and whether my colleague who was holding the fort for me had been able to cover the seven miles to her house in time he being, as we so often are in Devon, temporarily carless

But three hours of regained youth was worth having even though it did cost ten guineas Maybe I'll have it again in six months' time.

* * *

The discovery that rats which are given extra amounts of glutamic acid in the diet are more intelligent than their fellows on ordinary diet, and learn more quickly, and that milk is rich in glutamic acid, leads to some interesting speculations Can the rise of the mammals be actually due to, and not merely accompanied by, the appearance of milk glands for the nurture of the young, and can the growth in size of the brain and in intelligence be literally the cumulative effect of generations reared on milk? How much glutamic acid comparatively, does a snake consume? Or a bird? Can the emergence of *Homo sapiens* as leader of the mammals be due to a modification of the milk in the direction of more glutamic acid? It is not stated in your annotation of Sept 29 whether any comparative analysis of human milk and that of other mammals has been made from this point of view Folk wisdom has always maintained that more than physical nutriment is imbibed with the mother's milk

As between the primitive races and civilised man, milk alone cannot be so important a factor (since breast feeding is the rule among the former) as the general high food value of the white man's diet providing a relative excess of glutamic acid and probably other constituents not yet recognised as significant I do not know whether any detailed analytical comparison has been made between the milk of a well fed white woman and that of say an *Australian aborigine* Nowadays it may be hard to find the really well fed white woman.

But the rats have given yet another stimulus to one's ideas While the world shortage of food for human beings is being gradually overcome during the next year or two at least one constituent should be added to all diets and our research workers should turn all their energies to finding out what it is Just as a trace of manganese added to the diet is said to turn a cold

hearted female rat into a loving mother, so there may well be something analogous which will change a jealous and suspicious human into a friendly and coöperative person overflowing with goodwill to others. When this is found, let it be given first, and as soon as possible, mixed with plenty of glutamic acid, to all the members of the next International Conference

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Those who visit art galleries to look at the subjects of the pictures are admittedly a low form of life, but a doctor confronted with war pictures inevitably sinks into this class at times because so many of the scenes illustrate his own trade. Those who have regularly visited the National Gallery exhibitions during the war will find many familiar canvases among those now gathered for the Exhibition of National War Pictures in Burlington House Paul Nash's abstract luminous Battle of Britain, Stanley Spencer's tireless riveters, Henry Moore's shelterers—status discarded by a monumental mason—Edward Ardizzone's plump droll soldiers, Eric Kennington's incredible young men (in real life the male only wears that look of clear-eyed hunger for the Good, the True, and the Beautiful when one of his physical appetites is being denied, Kennington probably waits until they want their dinner), Laura Knight's rumpled parachute silk, and the spectral brilliance of the world seen by the late Eric Ravilious—these still take the eye But there is a professional interest for us in Evelyn Dunbar's nurses, who, with heads as flat as a python's, make camouflage nets or race through wards; in Elsie Hewland's nursery school, where the stout infants are a contrast to the wizened little Greeks, painted anachryl green for scabies; of Leslie Cole's scene in an orphanage, in Feliks Topolski's shadowy London Hospital staff, and in two solidly beautiful drawings by Robert Austin showing a sister washing out an Italian's eye and a bed patient having his nose packed They are pictures for realists, though; not one of them is rooted in abstract pattern, like Spencer's dockyards. Why is this? Is it possibly because dockyards leave most people emotionally neutral, while hospitals are often perturbing to those who do not work in them? The artists would say it was like our vanity to think so, but if there is anything in it, we shall have to wait until a Spencer crops up in the medical or nursing profession before we get to know how hospitals look on a different plane

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On the coast of the southern tip of Apulia, "where blue as any peacock's neck the Tyrrhene ocean shines," is a settlement of some 2500 displaced persons of 27 nationalities, housed in the little seacoast resort of Leuca di Bagni. The hygiene, medical inspection, and clinic work of the settlement is run by an American woman doctor of the US Public Health Service, helped by a Turkish and a Russian (woman) doctor, a Russian interpreter, one Tripolitanian and two American nurses, and two Albanian clerks In the hospital I saw, inter alia, a two-bed ward with an Ethiopian and a Turkish woman with tuberculosis, and the medical and nursing staff of the group of settlements included American, British, Canadian, Belgian, Czech, Turkish, and Italian doctors and nurses Can anyone beat that as a working international pot-pourri? Several asked for THE LANCET (advt charitable appeal).

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Of the great educative value of the opera in Rome, Naples, and Palermo—and no doubt since the spring in Milan too—to the British youth of both sexes we cannot speak too highly At a time when the love of music has been coming back into the nation a large number of our youths here had an opportunity of seeing opera at its best at prices within their scope in a way that no generation of young Englishmen and women have ever had before The Palestinian troops perhaps predominated in the audiences, but whether this was because of their hereditary love of music or the generosity with which their commanding officers had given them leave to go to Rome is unassessable How greatly our troops have profited from these operas may be illustrated by the story of the young ADMS who going over the Castello Sant' Angelo was all agog to see where Tosca threw herself into the Tiber, and when he found she could not have done this felt that Hadrian had cheated him

Parliament

ON THE FLOOR OF THE HOUSE

MEDICUS MP

DURING last week the Supplies and Services (Transitional Powers) Bill has passed through its stages from committee to third reading and has now gone up to the House of Lords. The Opposition have tried valiantly to reduce its operations to a period of two years instead of five, on which the Government have successfully insisted. The vote of credit for £2000 million agreed to without a division is, it is hoped, the last of these astronomical supplementary sums voted to defray the cost of Navy, Army, and Air Services and supplies Mr Dalton described it as a mopping-up operation Some mop!

In the debate on housing, important both in relation to immediate social needs and to Government policy, Mr Aneurin Bevan, the Minister of Health, and Mr. George Buchanan, Under-Secretary of State of Scotland, made a good impression on the House and, judging by the press, on the country The motion on which the debate took place, moved by Mr R S Hudson on behalf of the Opposition, was "That this House views with grave apprehension the shortage of houses in both urban and rural areas " No party disagreed on this in the House and no-one is likely to disagree with it outside In one London borough with a population of about 300,000 there is a waiting-list of 7000-odd And the waiting-lists exist everywhere The demobilised sailor, soldier, or airman wanting to return to his family would put the motion in shorter and more lurid language

Mr. Bevan was Churchillian in his grim portrayal of the situation There is no hope of a quick solution, and this winter will be hard The Government's policy is to treat housing as a military operation, and the Minister of Health showed that this was no mere form of words. Land for building is to be entered upon after 14 days' notice has been given on the land, and payment arranged afterwards Those fortunate enough to have more rooms than they are themselves using are invited to offer accommodation to others If the offer is not made voluntarily, recourse may be had to billeting The local authorities are to be entrusted with most of the work, for the greatest need, said the Minister, is among the lower income groups of the population who need houses to rent.

Today's problem, Mr Bevan affirmed, is the result of 25 years' neglect of housing. "We could have sustained the malice of the enemy and repaired the injuries inflicted by him on our cities" if it had not been for this neglect. The housing problem of the lower-income groups is to have precedence, but the income groups are not to be segregated as they have been. This segregation the Minister called "a monstrous infliction upon the essential psychological and biological oneness of the community" And he referred to the building of fretful fronts stretching along the great roads leading from London, belonging "to what one cynic called 'the Marzipan period,'" as part of the crimes against æsthetics by a long list of private speculators in house-building In future, the Minister hoped, there would be no segregation, either according to income-level or age-group.

Mr. Bevan is proposing to facilitate private ownership of houses by raising the limits under which local authorities can lend money under the Small Dwellings Acquisition Act But he warned the returning soldier not to be in a hurry to burden himself with a mortgage at the high housing prices now prevalent.

After 10 PM on Oct 17, Mr. H N Linstead raised the use of the term "Christian Science Nurse" by members of the Christian Science Church. Mr. A. Edwards, speaking as a Christian Scientist, said that these women received a thorough training. They did not practise in competition with other nurses and were employed only by Christian Scientists The Minister of Health undertook to try to get a form of words agreeable to all parties and on this the mover and seconder of the prayer withdrew their motion. As one who uses Christian Science in the treatment of disease is called a Christian Science practitioner, why should not the assistants be called "Christian Science Helpers"?

FROM THE PRESS GALLERY

The Dearth of Nurses

IN the House of Commons on Oct 16, on a supplementary vote of £130,000 for the Ministry of Health, Mr C W KEY, parliamentary secretary to the ministry, said that a fresh attempt was being made to increase the number of sister tutors in order to train more student nurses The existing grant of 50% to hospital authorities for the training of sister tutors would be continued and grants would now also be given to individual nurses for the same purpose leaving them free to fill sister tutor posts at any hospital they liked afterwards Many ex Service men and women, and recruits from industry, would enter nursing at a higher age than that at the appropriate point in the Rushcliffe scale and it was proposed to give them for 12 months a grant in addition to the amount they received under the Rushcliffe salaries award These two sums would amount to £7000

Arrangements had been made with the Women's Voluntary Service to set up some hostels as an experiment where domestics could live during training, and while supplementing the domestics in the local hospitals The sum involved for this purpose was £5000, but it was expected that the hostels would ultimately become self supporting, because the domestics themselves would be paid fees for their board and lodging

Through the transfer of American troops, some temporary hospitals were falling vacant and in view of the need of hospital accommodation it was proposed to give the local authorities a grant for the maintenance of these hospitals equal to about half of the expenditure That would involve some £10,000 During the war emergency maternity homes in evacuation areas had provided some 3500 beds, in which 150,000 births had taken place It was proposed that these homes should now be taken over by the local hospital authority concerned, or by the voluntary hospitals, and run for maternity purposes This would involve an expenditure of £224,000, but as the beds would be charged to the local authorities at the average figure per day of maintenance, and to the voluntary hospitals at something like two-fifths of the expenditure involved, there would be a sum of £217,000 which would be written off against the £224,000, leaving £7000 to be met

Housing

In the House of Commons on Oct 17, replying to a motion raised by the Opposition, Mr A BEVAN, the Minister of Health, made an important statement on the Government's housing policy

The needs of the lower income groups, he affirmed, would be met in the first place mainly through the local authorities, the provision of houses to let being kept in the forefront. Local authorities however, would be allowed within a limited time to license the building by other agencies of houses costing up to £1200, or £1300 in London Local authorities would be authorised to use land for building in advance of the conclusion of negotiations on the question of terms He emphasised that he was not prepared to give promises about the number of houses which would be built within any given period; he was not going to do any crystal-gazing At the same time he was hopeful that the shortage would be relieved in four years. To keep Parliament constantly informed of the rate of progress he undertook to issue monthly reports from the beginning of next year He proposed to make an appeal to those possessing more housing accommodation than they required to share it this winter with others in need It was his desire that this might be done on a voluntary basis, but local authorities would be armed with power to requisition accommodation if necessary It was the intention of the Government to replace the Housing (Rural Workers) Act with a new and better measure He was sympathetic about the reconditioning of certain types of cottages But to meet the immediate emergency he wanted all the building labour in rural areas for the construction of new houses. Mr Bevan denied that he had any objection to the private ownership of houses, and announced the forthcoming introduction of legislation raising the limits within which local authorities could lend money for acquisition of dwellings. The Ministry of Supply would be used to provide housing equipment, and the Ordnance factories would be used to supplement the output of private industry Mr Bevan assured the House that he was fully aware of the serious housing situation which would arise during the coming winter, and the suffering and hardship that it might cause, but he believed that in a few years the back of the housing problem could be broken

Parliamentary Medical Group

A meeting of the Parliamentary Medical Group was held at the House of Commons on Oct 18 when the following office-bearers were elected Dr Haden Guest, chairman; Mr H Linstead (secretary of the Pharmaceutical Society) secretary; Sir Henry Morris-Jones, treasurer Dr Haden Guest will continue to represent the group on the Central Medical War Committee

QUESTION TIME

Medical Man-power

Mr D L LIPSON asked the Secretary of State for War what was the present ratio of medical officers in the Forces to Army personnel; and how this compared with the present proportion of doctors in this country to the civilian population —Mr J J LAWSON replied: The present ratio of RAMC medical officers in the Forces to personnel under their medical charge is 2 57 per 1000 All effective medical officers whether engaged on administration, hygiene hospital work or attendance on unit sick, are included in the ratio I understand that the present proportion of doctors of all kinds in this country to the civilian population is 0 74 per 1000 I should however point out that circumstances and conditions in the Army and civil life are so different that any true comparison is impossible

Sir G Fox asked the Under-Secretary of State for Air whether he was aware that the present strength of medical officers in the RAF was 2 27 medical officers per 1000 men, which compared with 1 doctor per 3500 of the civil population why it was necessary for the proportion of doctors in the RAF to be 8 times that for the country as a whole now that war time conditions no longer prevailed; and whether he had a plan for the rapid release of doctors from the RAF to take up vital work on the home front —Mr J STRACHEY replied The comparison in the first part of the question requires further explanation in that the ratio given for the Air Force includes doctors employed in hospitals on research and on administration as well as those on RAF stations at home and abroad On the other hand, the civilian figure for this country, which I understand is about 2500 per doctor and not 3500 as stated in the question, relates to general practitioners and excludes doctors working only in hospitals on public health administration, and on research A similar figure for the Air Force would be 1 in 1000, out of which provision has to be made for a doctor at each active airfield This ratio is less than was provided in peace time The distribution of medical man power is now under review by the Government

Supply of Surgical Dressings and Liquid Paraffin

Dr L. COMYNS asked the Minister of Supply and of Aircraft Production if he was aware that the residents of Silvertown, West Ham had difficulty in obtaining surgical dressings and liquid paraffin and would he take steps to ensure that reasonable supplies would be available at the earliest opportunity.—Mr J WILMOT replied: I am not aware of any particular difficulties in Silvertown in the supply of either surgical dressings or liquid paraffin The production of surgical dressings is now sufficient to meet demand During the summer there were local shortages, due mainly to large movements of population, but steps have since been taken to remedy this position. Supplies of liquid paraffin are ample for medicinal use

Grants for Leprosy Relief Work

Mr D L. LIPSON asked the Secretary of State for the Colonies if he was aware that the amount contributed by the Government for the welfare of the 2 100 000 lepers in the British Empire is insufficient and had to be supplemented by private charity; and would he take steps to increase the amount to ensure that everything possible was done for these unfortunate people —Mr GEORGE HALL replied: Although accurate figures are not available my information is that a maximum of 700 000 out of the number of lepers mentioned live within the Colonial Empire; of these the greater part are in Nigeria. Expenditure from Government funds on leprosy relief work in the Colonies generally is increasing In Nigeria a big anti-leprosy campaign is now being under

taken A grant of £258,000 for this campaign was approved last year from the Colonial Development and Welfare Vote, and a sum of £5000 per annum for a period of five years is being contributed by the Nigeria government An application by the Nigeria government for a further £170,000 from the Colonial Development and Welfare Vote is at present under consideration

Sickness Benefit

Mr N A BEECHMAN asked the Minister of National Insurance whether, in view of the delay which must inevitably occur before the passing into law of a comprehensive scheme of national insurance, he would forthwith introduce measures to bring the exceptionally low rate of sickness benefit into conformity with unemployment and other benefits, and at the same time extend to all cases of sickness, provision for dependants as recently made available in the case of tuberculous patients —Mr JAMES GRIFFITHS replied Partial legislation on this matter in advance of the main insurance measure would be unsatisfactory, but it is the Government's intention so to frame the main legislation that the earliest practicable opportunity may be taken of bringing into effect, as part of a general plan, the improvements in rates and conditions of health insurance benefit which it will propose It is proposed to introduce the major Bill early in the new year and to press forward so that it may be passed into law during this session

Tuberculous Service Men

Major E A LEGGE BOURKE asked the Secretary of State for War whether he had any plans for the care and treatment of pulmonary tuberculosis in officers and men returning from overseas beyond that at present available in civil hospitals — Mr J. J LAWSON replied The possibility of treating Service tuberculosis patients in Service hospitals or Service wings of civil sanatoria is being examined with a view to minimising any delay between diagnosis and the institution of appropriate treatment

Help for Ex-Service Medical Students

Mr S HASTINGS asked the Minister of Education if any special arrangements had been made for the training of selected ex Service personnel for the medical and dental professions —MISS ELLEN WILKINSON replied Assistance under the Government's Further Education and Training Scheme would be available in suitable cases and subject to the usual conditions to ex Service men and women wishing to study medicine or dentistry

Training of Nurses

Mr F MESSER asked the Minister of Health if he had considered plans for the reduction of the period of training for the State-registered nurse, and if he had any statement to make in regard to it —Mr BEVAN replied This is a matter primarily for the General Nursing Council, which is the statutory body responsible for framing rules relating to training for State registration I understand that the council are considering the possibility of revising the basic training for State registration

Tuberculosis Nurses

Mr MESSER asked the Minister if, in view of the shortage of tuberculosis nurses, he would negotiate with the General Nursing Council with a view to securing the recognition of the TA certificate, so that such nurses could be placed on the supplementary register —Mr BEVAN replied The General Nursing Council have already been approached on this matter and are not prepared to admit persons possessing the TA certificate to a supplementary part of the register unless they are also general State registered nurses I do not feel able to adopt the suggestion, since I am advised that it would at present hinder rather than help recruitment for tuberculosis nursing

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A LIGHT touch is a change in a diet book *The Cookery Book for Diabetics* (Diabetic Association Lewis Pp 82 4s) contains all the necessary material for planning and arranging a varied, even luxurious, diet, and the introductory lessons in food values are presented and illustrated in a pleasantly impish way The recipes introduce a wide range of interesting dishes most of them within the range of foodstuffs available in this post-war world Everyone catering for diabetics would like this book in the kitchen

Letters to the Editor

THE MENTALLY DISABLED

SIR,—As noted in your annotation last week, the Ministry of Labour have now opened the register of persons handicapped by disablement and are inviting all such persons to apply for registration as soon as possible The conditions for registration are

1. That the person suffers from a disability of any kind which handicaps him in obtaining or keeping employment, or undertaking work on his own account, of a kind which otherwise would be suited to his age, experience, and qualifications
2. That the disability is likely to last for six months or more
3. That the patient is nevertheless reasonably capable of work

Under the quota and designated classes of employment schemes, certain vacancies in employment will have to be filled by a registered disabled person Sheltered employment may be provided for the seriously disabled.

It seems that in deciding whether a person is eligible for registration or not, the disablement rehabilitation officer (DRO) will be very much guided by medical reports from the hospital or from the patient's family doctor, although reference may be made to a doctor appointed by the Ministry of Labour or to a panel of the local disablement advisory committee If it is true that a large proportion of all disability, and of chronic disability in particular, is due to handicaps of a psychiatric nature, a considerable responsibility will fall on psychiatrists generally in connexion with applications for registration I am writing this letter because I have seen little or no discussion about which types of psychiatric conditions should be considered suitable for registration and which should not It would be unfortunate if psychiatrists followed widely different general policies and if in one area many patients were registered and in another area few

At the Royal Edinburgh Hospital for Mental and Nervous Disorders, under the direction of Prof D K Henderson, we have found, under the interim scheme that in many cases it is enough if the patient is resettled in suitable work by the DRO, and in these cases actual registration is not necessary. Registration as a person handicapped by disablement might sometimes implant a fear of prolonged disability in the minds of suggestible patients On the other hand, there are many patients who will benefit from the protection of being registered—such as those suffering from mental deficiency, from epilepsy, from mild but lasting enfeeblement after a psychotic illness, and from the more chronic neurotic states In the last analysis, of course, the decision will be based not on the formal diagnosis but on the circumstances of the individual case

In recommending patients for registration one may offer advice about the type of work considered suitable, which will include sheltered employment when it becomes available We must not expect the DRO to be able to resettle any and every patient, and we must adhere to the condition that the patient must be "reasonably capable of work" Some psychopathic states may be excluded from the register as "habitual bad characters"

I should be glad if other psychiatrists would express their views on how we can best be guided in recommending patients for registration, so that a common policy may be developed, and so that we may properly discharge our responsibilities to our patients and to the Ministry of Labour

Morningside Place, Edinburgh HARRY STALKER

THE STRAINED BACK

SIR,—I read with great interest the three articles by Dr Crisp, Dr Cyriax, and Mr Burns and Mr. Young (Oct 6) and congratulate you on your editorial comment in which you temper their diverse views to that degree of moderation with which every new proposition must be viewed

Dr Cyriax's view that acute lumbago is a manifestation of derangement of the articulations of the vertebræ or even minor disk injury is startling, while the number of disk injuries seen and proved at operation by Mr. Burns and Mr. Young in patients suffering with backache is remarkably high.

For many winters I have been partially incapacitated with sciatica for a week or so This always resolves with a few treatments of diathermy given by one of my hospital sisters It now appears that I must be suffering from a disk lesion, but I certainly don't want a laminectomy In one patient, a backache which hitherto from my orthopædic training I would have called a postural lumbar lordotic ache, can be readily cured by several sharp blows on the back in a flexed position, or by the manœuvre described by J J Keegan (*J Amer med Ass* 1944, 126, 808)—laying the patient on the floor and forcibly flexing the hips three times, following this with forced hyperextension combined with traction movements I must now visualise that instead of just loosening up the sacro iliac ligaments these procedures must replace minor degrees of disk herniation.

Are we not going too fast in disk pathology, judging by the trend of these articles?

Wimpole Street W1 G O TIPPETT

AIR EVACUATION IN NORTH-WEST EUROPEAN CAMPAIGN

SIR,—I have read with interest Major K D Stewart's article in your issue of Sept 1 As senior medical officer of the Transport Command group which carried out the air evacuation of casualties from the 21st Army Group theatre of operations, I would like to make one or two comments

Firstly each CAEC (casualty air evacuation centre) on the home-based airfields in the United Kingdom had a capacity for 200 cases and could in an emergency filter up to 400 cases through in a day's evacuation The highest number of casualties arriving during any one day from the Continent was 934

The first air evacuation of casualties from the British sector of the bridgehead was on D + 7 (June 13)

The incidence of airsickness among the casualties was low, being a little over 1 2% Of those airsick, the majority were the walking wounded who sat in the rear of the aircraft

Between D-day and VE-day 116,700 casualties were evacuated by this group without the loss of a single casualty Of these 77,365 were brought to UK from the Continent, and 39,335 were carried on the Continent from the advanced airfields to those in the base areas.

R C. JACKSON

THE NURSING CRISIS

SIR,—It seems to me that the General Nursing Council must be made to review its regulations and stipulations

In six years in the Royal Air Force I have come across many male and female orderlies (RAF, RAMC, and WAAF) who had an excellent practical knowledge of nursing, who are keen on nursing, and who would like to continue nursing One girl recently asked me to see what I could do for her, as she wished to become a State-registered nurse She has done six years, and for five of these years she has been working in a RAF hospital She has been doing work, in the last three years, equivalent at least to that of a last year probationer, and sometimes with more responsibility, for she has been in charge of the ward in the absence of the sister Her practical knowledge is at least equal to that of one who has been training for three years in a hospital recognised by the General Nursing Council I wrote to a hospital asking the conditions under which she could be taken in. The reply I received was that if she wished to be a State-registered nurse she must start again from the beginning, become accepted as a probationer, and go through a further three years' training Quite recently the General Nursing Council has stated that it will give such people six months' credit That is a meagre and entirely inadequate gesture Here is a girl typical of many, who is being discouraged from taking up nursing and becoming qualified Surely she should be allowed to sit an examination, and according to the standard she shows in that examination she should be assessed the further training required before she can sit her State registration examination As I say, *she is typical of dozens of men and women* whom I have met and who are anxious to continue nursing

I had the privilege, when I was senior medical officer of one of the large liners lately in use as transports and we were laid up in New York for six weeks, of taking my entire British staff to an American county hospital With some temerity I told the medical superintendent that my orderlies were up to the standard of pregraduate nurses They were employed as such The medical superintendent (or, as they call him, the director) of this hospital of 850 beds, and the matron, expressed to me their amazement at the efficiency of our men, who in their opinion were above the standard of graduate nurses in America Yet these men, if they wish to become State-registered in this country, have got to start all over again

It seems to me that it is time that a drive was made to make the rather-rigid General Nursing Council alter its standards and its outlook

ESSE QUAM VIDERI

A COMPREHENSIVE TRAINING COURSE FOR NURSES

SIR,—Dr Peirson's letter in your last issue marks a great step forward in nursing education But it is a pity that psychiatric training is not made compulsory for the mind is important in all illness and more amenable to treatment than the body Moreover, one-third of illness is psychosomatic

While I do not deery the importance of such specialties as fevers, pulmonary tuberculosis, and orthopædics I feel it is possible that the nurse may never have such cases to care for in her postgraduate career; but every single patient she nurses will have a mind.

Central Hospital, Warwick E S STILES

THE OPERATION FOR VARICOSE VEINS

SIR,—The comparatively new operation of ligature and injection of varicose veins is steadily becoming established Long term results come forward slowly, because a period of three to five years must elapse before each step can be evaluated From time to time further points arise, and it is therefore necessary for those who have worked, talked, and written on this procedure to "pool" the information as it comes to hand In December, 1944 (*Brit med J* ii, 814) I advocated the operation of ligature and injection at the groin and ankle I would like to report several items which have come to my notice in connexion with this operation.

(1) *Postoperative painless hæmaturia*—The operation is occasionally followed in 24 hours by painless hæmaturia—I know of five cases. Sometimes blood appears at one or two acts of micturition, at others throughout the day Another surgeon has told me of a similar case It has followed the injection of 30% saline and also of Ethanolin There were no further ill effects.

(2) *Ligature and division of the internal saphenous vein in the groin*—In ligaturing the internal saphenous vein in the groin it has been the custom to tie the lower end of the vein once but doubly tie the upper end I have seen the ligature on the lower end slip It was caused by the bursting effect of the injection of 20 c.cm of 30% saline at the ankle It would appear necessary to transfix both divided ends of the internal saphenous vein in the groin when it is injected at the ankle and to make the upward insertion slowly Further a large incision must always be made to ensure that the internal saphenous and its branches are tied and to avoid ligature of the femoral vein or even of the femoral artery

(3) *Incompetence of the external saphenous vein* is at times seen without the internal saphenous vein being apparently affected Follow-ups have shown that if the external saphenous vein is ligatured and injected at the popliteal space and the internal saphenous vein is not treated then later on the internal saphenous vein becomes affected and needs ligature and injection Therefore it is probably right to ligature and inject the internal saphenous vein in all cases of varicose veins where there is incompetence of the external saphenous vein or of the communicating veins.

(4) *Subsequent injections*—Occasionally after the remedy of ligature and injection at the groin and ankle one or two lengths of vein remain unscleroised and these require subsequent injection I use ethanolin for this and the amount needed is 1-2 c.cm; larger doses tend to be followed by gross painful and temporarily incapacitating reactions

The ethamolin should be used from ampoules, not from a rubber-capped bottle

(5) *Pulmonary embolism*—I am aware of this occurring in 2 patients in a series of 570 One caused an illness of six weeks, another of ten days There may doubtless have been other instances The preventive measure seems to be scrupulous aseptic technique and to get the patient out of bed the day of operation The operation is a major procedure, minor operating theatre technique is dangerous When the veins are gross in both legs it is advisable to deal with only one leg per session

(6) *The scars after ankle incisions*—For a few weeks after ligature and injection at the ankle the scar is visible through silk stockings, and here again lies the need for accurate closing of the wound to avoid "eyesores," and disrepute to a first class operation

(7) *Deaths after operation*—Dr Foote recently reported a death following ligature and injection of varicose veins, and in a personal communication told me of his knowledge of it in the practice of other surgeons So far it has not occurred with me, but no doubt I have only to keep on doing the operation and I will have the experience Knowing this, remarks on the prognosis of the operation must be appropriately expressed

Finally, I would urge the necessity for giving full time to the operation, it is more than a minor procedure—*one leg may take 20–45 minutes*—but the sessions are richly rewarded by the improvements bestowed on patients

Harley Street, W1 HAROLD DODD

DEAD HAND IN USERS OF VIBRATING TOOLS

SIR,—May I, as a physiotherapist, put forward a suggestion for prophylaxis and treatment of Raynaud's disease due to industrial causes? The article by Prof E D. Telford, Dr M B McCann, and Dr. D H. MacCormack, in your issue Sept 22, interested me particularly because I have had the good fortune to treat several cases of Raynaud's disease by short-wave diathermy with some excellent results

The fact that this condition in industrial workers appears to be induced by the use of vibrating tools, on which a great deal of pressure is used with the left hand, seems to suggest that the continued pressure predisposes to a vasoconstriction of the vessels of the hand Short-wave therapy is known to produce a deep pyrexia, and to be a vasodilator and an analgesic to the sensory and autonomic nerves

Various suggestions are made in the article as to prophylactic measures, which are mostly of a mechanical nature, another is that workers should not be allowed to continue in this work for longer than six-monthly periods I would like to suggest that these workers be given a course of short-wave treatment at the beginning of their working period and a further course about the middle of the term

London, W1 GINA A. TAYLOR.

HYPOPIESIA

SIR,—Since my retirement from the active staff of the Norfolk and Norwich Hospital in 1939 I have refrained from entering into any polemical clinical discussions But I cannot refrain from combating the pessimistic prognosis of cases of hypopiesia as set forth in your issue of Oct 20 by Dr Piesch From many of his morbid statements on this subject I quote the following.

> "In my experience low blood pressure *statistically* involves more dangers and more serious complications than high blood-pressure I am thinking here especially of the dangers of thrombosis and embolism, cramps, &c In this point I believe every observant practitioner will agree with me"

In 1940 the late Sir Humphry Rolleston asked me to write for the *Practitioner* a paper on hypopiesia which was published in the February, 1941, number and later was incorporated in a Practitioner Booklet, "Disorders of Blood-pressure," 1942 For the preparation of this paper I spent a considerable time in analysing many tables of life assurance societies, both English and American, all of which showed that people with low blood-pressures had a longer expectation of life than those with normal or raised blood-pressures Thirty years of cardiological work has convinced me that this is correct

In the same paper I discussed the question of vasovagal attacks and described some cases of outstanding interest, all of which had an emotional basis *associated* with hypopiesia Although twenty years have passed since these patients first came under my notice, the majority of them are still alive and in good health; the others died at ages above 70 years In the hundreds of cases with simple hypopiesia not associated with dramatic vasovagal attacks my optimistic prognoses have proved to be sound Providing that the candidate was otherwise sound, I should not dream of giving him a poor assessment for life assurance merely because his blood-pressure was lower than the so-called normal

Norwich H J STARLING

PENICILLIN CREAMS

SIR,—There are two points I think might be added to your annotation of Oct 13

We have used both 'Lanette Wax SX' and 'Eucerin LM' and have now discarded the former oil-in-water emulsion (except for sensitivity tests) in favour of the latter water-in-oil preparation It is not only difficult, as you say, "to visualise the liberation of medicament at any reasonable rate from the water-in-oil type" but it is difficult to demonstrate it For routine tests we place a small portion of a lanette-wax/penicillin emulsion on the surface of the culture medium, but eucerin LM/penicillin cream tested in this way appears inert, and has been discarded by some workers on that account, because the penicillin is not easily liberated It is, however, very rapidly liberated by a simple technique devised by my senior technician, Mr G Phillips. A circle of sterile wet filter-paper about 5 mm. in diameter is placed on the medium, on this a loopful of eucerin LM/penicillin cream is placed The resultant area of growth inhibition with the standard staphylococcus is up to the usual size. The success of this very simple device suggests that in contact with a moist surface, which will include almost all lesions for which penicillin is used, the penicillin is rapidly released—as indeed clinical use indicates. Eucerin LM provides an easily spread cream and we are satisfied that it yields up all its penicillin.

A second point is that these ointments retain their potency longer than is generally believed We have batches of both which have been kept in the refrigerator for over six months and still show more than two-thirds of the original strength

Kingston-on-Thames D STARK MURRAY

IS THERE A SHORTAGE OF DOCTORS?

SIR,—In 1935 I began general practice in a partnership In 1936 I passed the DA examination, being, I think, the first in my county to do this There was a local cottage hospital of some 24 beds, and it was not unreasonable that I should anticipate being put on the staff as an anæsthetist, especially since a clue to the standard of anæsthetics is given by the fact that they had neither a Boyle's machine nor an intratracheal tube in the building However, my first routine hospital anæsthetics after this were given in June, 1940, in a new municipal hospital, nine miles away Two months later I was employed by the EMS whole-time at this and another hospital nearby A year later my EMS work was part-time and I returned to my practice; but I was still excluded from the local hospital

At this time a London consultant came down to operate on one of my patients He requested that the patient should be intubated; even the offer of moral support and a laryngoscope did not persuade the senior anæsthetist to undertake this, though he accepted a fee for standing by as the hospital anæsthetist whilst I gave the anæsthetic

In 1942, for medical reasons, I gave up general practice and devoted my time to anæsthetics only I was subsequently appointed to two London hospitals—one a teaching hospital In 1942 the rules at the local hospital were altered for the duration so that all local GPs were on the staff. A telephone call to the medical

secretary confirmed that this excluded me It was reasonable to believe the statements of the local doctors that they were overworked ; as I was not overworked I wrote to the secretary of the cottage hospital offering my services as anaesthetist, and suggested that this would free other doctors from time in the theatre I had a very courteous reply assuring me that they had all the anaesthetists required

And so we reach the astounding situation that during the war I have anaesthetised cases for many of the leading surgeons of the day—I have been a regular member of a surgical team that can claim really to have saved many lives—but I am the only local doctor who is not allowed to give an anaesthetic at the local hospital ; and even though patients have specifically asked for me their request has been refused

How can I do anything but look to the Ministry of Health and the county council for better planning and a squarer deal in the future, and be very dubious when I hear these bodies condemned out of hand, and the voluntary hospital system lauded as the only good one?

D.A

SHOULD THE BRACHIAL PLEXUS BE EXPLORED?

SIR,—I am most grateful for Professor Seddon's criticisms. I realised that it is impossible to assess the final value of these operations owing to the inevitable slowness of recovery But since I have already had two recoveries out of eight consecutive cases, I feel that every brachial plexus injury due to missiles should be explored

Royal National Orthopædic Hospital E HAMBLY

On Active Service

AWARDS

OBE

Lieut Colonel J C ANDERSON MB ST.AND , FRCS RAMC
Lieut -Colonel W S C COPE MAN MD CAMB FRCP RAMC
Colonel J P DOUGLAS MBE MB ST.AND RAMC
Lieut -Colonel ROY EVANS MRCS RAMC
Colonel F G FLOOD MC MB DUBL, late RAMC
Lieut.-Colonel F N FOSTER, MB LEEDS, FRCS, RAMC
Lieut.-Colonel EDWARD HUTCHEON MB ABERD RAMC
Colonel J P J JENKINS MRCS RAMC
Lieut -Colonel A B KERR MB GLASG FRFPS, RAMC
Colonel H E KNOTT, MD DUBL., RAMC
Lieut -Colonel W R LOGAN LRCPI LDS RAMC
Colonel F McL. RICHARDSON, DSO MD EDIN., RAMC
Colonel R G SHAW MC MB EDIN late RAMC
Colonel G G TALBOT MB NZ, FRCS RAMC
Colonel C F ABBOTT RCAMC
Lieut.-Colonel DONALD CAMPBELL, RCAMC
Lieut.-Colonel K. J COATES RCAMC
Lieut -Colonel C D S LEEP RCAMC
Lieut -Colonel JOSEPH TANNAN RCAMC
Colonel C. G WOOD RAOMC

MBE

Lieut -Colonel W E. A BUCHANAN MB GLASG., RAMC
Captain K. G. BURROW MRCS, RAMC
Major J D FINLAYSON MB GLASG., RAMC
Major R B HUNTER, MB EDIN RAMC
Major D J JOHNSON MRCS RAMC
Major W L KINNEAR MD ST.AND RAMC
Lieut -Colonel J C MACKAY MC, MB EDIN RAMC
Major WILLIAM MICHIE, MB ABERD FRCSE, RAMC
Major R O MURRAY MD CAMB., RAMC
Major R. O G NORMAN MB CAMB., RAMC
Major W A McKIBBON RCAMC
Major EDWARD WOLSTENHOLME RCAMC

MC

Captain JOHN BURNS MB, RAMC
Major J L. CHISNALL, MB LPOOL, RAMC
Captain R D S JACK MRCS, RAMC
Lieutenant RODERICK MACKAY MB ABERD RAMC
Lieutenant D J MACRAE MB ST.AND RAMC
Captain G D H McQUITTY MB ST AND RAMC
Captain ISAIAH MORRIS, MRCS RAMC
Lieutenant F W M PLANT MRCS RAMC
Captain JOHN SHEEHAN MB NUI RAMC
Lieutenant G F STOKER, MRCS RAMC
Captain K. A CAMPBELL, RCAMC

MENTIONED IN DISPATCHES

Lieutenant G H PARKE MB LOND FRCSE, RAMC
Major C H INGIE MB ST AND., RAMC
Captain J MORRISSEY RAMC (killed in action)
Captain A TAYLOR SMITH MB EDIN

Obituary

WALTER BRADFORD CANNON

CB, M D HARVARD, S D, LL D

Professor Cannon, whose death on Oct 2 at the age of 73 is reported from New Hampshire, started his fruitful career early While he was still a student at Harvard in the 1890s, and before he graduated in medicine, he realised the potentialities of the recently discovered X rays, and in 1897 was able to report to the American Physiological Society the results of his investigations on the movements of the cat's stomach, as revealed by X ray photographs of a meal containing bismuth subnitrate The importance of this pioneer work, which laid the foundation of the radiology of the alimentary tract, requires no emphasis

Cannon had received an arts degree in 1896 and graduated in medicine in 1900 It was only natural, after such a promising beginning, that physiology should claim his interest, and he spent six years under H P Bowditch, one of the founders of the American Physiological Society whom he succeeded in the George Higginson chair of physiology at Harvard in 1906 In 1911 he published a monograph whose title, *Mechanical Factors of Digestion*, epitomises his interests up to that time Thereafter for many years, with the exception of those devoted to problems of shock during the first world war, his attention was focused on the functions of the suprarenal medulla and the sympathetic nervous system In this field his investigations on the one hand brought him into contact with psychology and on the other led to a masterpiece of surgery—namely, the removal of the whole of the sympathetic nervous system in cats His famous book, *Bodily Changes in Pain, Hunger, Fear and Rage*, published first in 1915, and again in 1929, by which time it had ceased to become controversial, introduced a generalisation of the highest importance regarding the emergency function of the sympathetic-adrenal system and its bearing on the emotions. His later works, *The Wisdom of the Body* and a number of papers and lectures, show a development of interest along ever broadening paths, which finally centred round the subject of "homeostasis," his own collective name for the integration of all those functions of the body which confer upon it immunity to changes in its environment His last popular work, delivered as a lecture in 1940 to the American Association for the Advancement of Science and published as a pamphlet in this country under the title of *The Body as a Guide to Politics* attracted a good deal of attention. His careful researches had, however established a scientific fact of a more particular nature—namely, that most peripheral sympathetic nerve-endings act in virtue of a substance, closely resembling (if not identical with) adrenaline, which Cannon christened "sympathin" Today the humoral transmission of nerve impulses is one of the most important topics in physiology, and the actions of sympathin's opposite number, acetylcholine, have placed important weapons in the hands of the clinician

Cannon had many distinctions conferred upon him including honorary doctorates from the universities of Yale Liége, Strasbourg, and Paris He was a foreign member of the Royal Society, before which he delivered the Croonian lecture in 1918 He was Linacre lecturer at Cambridge University in 1930 and Baly medallist of the Royal College of Physicians in 1931 In 1931 he was made one of the honorary members of the Physiological Society, of whom there are seldom more than a dozen at any one time He was president of the American Physiological Society in 1914 and of the American Association for the Advancement of Science in 1939 and he served for many years on the National Research Council of the United States In recognition of his services during the last war, for part of which he

was attached to the British military service, he was appointed CB in 1919

Personally Cannon was known for his tolerance and patience and his imaginative and stimulating conception of the development of physiology He had a reputation for epigram and his literary style was vivid He retired from his chair at Harvard in 1942.

GERALD QUIN LENNANE

MC, FRCSI, DPH

By the death on Sept 12 of Dr. Lennane, former medical officer of health of Battersea, the public-health service lost a wise and helpful colleague, always ready to show kindness or dispense hospitality Born in 1869 in Galway—his forebears were named after a village in co Galway—he was trained at Ledwich medical school and the Royal College of Surgeons, Dublin, and at King's College, London, qualifying LRCPI in 1891 After house-appointments at Jervis Street, Mater Misericordiæ, and other Dublin hospitals, and a spell as surgeon to S S *Massachusetts*, he took his FRCSI and his DPH in 1900 and for a few years was in general practice in Battersea. In 1906 he was appointed MOH to the borough In 1914, at the age of 45, he volunteered for service in the RAMC and was attached to the First Division, BEF, being mentioned in despatches in 1916 and awarded the MC in 1917 He was a highly popular and efficient as well as a courageous officer, and after his demobilisation he was appointed examiner in hygiene at the Royal Army Medical College, an appointment to which he gave devoted service until 1934 Dr James Fenton, writing in the *Medical Officer* for Oct. 13, recalls that it was Lennane's custom to get in touch with newly appointed medical officers of health of the metropolitan boroughs and offer his advice in overcoming the difficulties of a newcomer. In this way many of his junior colleagues profited by his wisdom and wide experience of local government, besides enjoying the generous hospitality which was his especial pride. In the debates of the Metropolitan branch of the MOH Society he displayed an endearing old-world courtesy in addition to a wide knowledge, and in 1926 he was elected president In Battersea he was highly respected by the councillors and by his brother officers and staff for his courage in tackling public-health problems. After his retirement in 1934 ill health cut him off very largely from his friends and associates

Dr Lennane had three sons, the eldest of whom is medical superintendent of Bretby Hall Orthopædic Hospital, and two daughters

ARTHUR AMBROSE LISLE WEBB

KBE, CB, CMG, MRCS, DPH, DTM

Sir Lisle Webb died on Oct 7, at the age of 74, at his home at Balcombe, Sussex. His medical school was University College, of which he subsequently became an honorary fellow, and, after qualifying in 1895, he went as district surgeon to Basutoland On the outbreak of the South African War in 1899 he received a commission as lieutenant in the RAMC, and in the next twenty years he made distinguished progress in the Corps He obtained the diplomas of public health and tropical medicine, was major in 1911 and lieut -colonel in 1914, and in 1915 was appointed CMG In the next year he became deputy assistant director-general of Army Medical Services, and in 1917 assistant director-general In 1919 he was made CB, and his experience and administrative talents singled him out as appropriate to take charge of, and develop, the medical services of the Ministry of Pensions, which, with the end of the war, was faced with immense responsibilities He became its director-general early in that year, and in 1920 was appointed KBE

As the first director-general of the fully constituted medical services of the Ministry of Pensions, Lisle Webb had a difficult task The clinical problems in the entitlement to, and assessment of, pension under the royal warrants were largely new to the profession, and moreover needed an approach on lines of thought somewhat foreign to normal medical practice It was Lisle Webb's work to build up a team of whole-time and part-time doctors who could tackle and advise on these problems with sound judgment and administrativ ability, in friendly coöperation with lay colleagues an with the profession as a whole He had to arrange fo medical boards on a vast scale, in the year 1921 the numbered 1¼ millions He had to make provision fo the treatment in hospitals and at clinics of very larg numbers of men suffering from many different condition Special provision was needed for facial injuries, tropica diseases, and nervous disorders, artificial limbs an surgical appliances had to be supplied, and scheme devised for combining treatment with training I 1921 the number of pensioners who received institutiona treatment was 130,000, and 20,000 artificial limbs we issued These details indicate the wide scope of th organisation which had to be developed throughou the country

Lisle Webb organised briskly and efficiently H control was felt as personal, he knew his staff, and the knew him He was approachable, understanding, an human He would accept advice and listen to contrar views, but yet keep steadily to his main line of actio The smooth working of his medical services, and the continued efficiency and adaptability in changi circumstances through many years, justified his polic A kindly man, who did not pretend to qualities he d not possess, he gained the affection and confidence of h staff Off duty, he delighted in the life and livesto of his farm

In 1933 he retired from his post as director-gener and was appointed honorary consultant physician the Ministry. He was also appointed treasurer a secretary to the governors of Queen Mary's Hospit Roehampton, a position which enabled him to keep touch with his old colleagues During the followi years there were considerable extensions at Roehampto in which he took keen and active interest Faili health led to his giving up this work in 1942 His wi died three weeks before him, they had no children

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WORK OF THE PERMANENT CENTRAL OPIUM BOARD

THE latest report of the Permanent Central Opium Boa to the Council of the League of Nations reviews their work the international control of trade in narcotic drugs since t beginning of the war Despite enormous difficulties t organisation of the Board was maintained and collaborati with most of the participating governments was preserve Headquarters were temporarily transferred from Gene to Washington but have now returned There was a serio decline in the statistical returns annually received from 15 to 965 in 1941, but this year they will probably be over 15 from 49 metropolitan countries and 66 territories. The chi defaulters are the Axis and Axis occupied countries Neve theless it is claimed that the end of the war "finds t Treaties unimpaired"

Spain, though party to the conventions of 1925 and 193 has persistently flouted the requests of the Board, has su plied no statistics, and has persistently imported drugs excess of estimates Collaboration with Soviet Russia producer, manufacturer, and consumer will, it is anticipate be promptly resumed Turkey has continued faithfully comply with its obligations, but Iran, a larger producer raw opium, has never ratified the convention of 1925, wh its returns, under that of 1931, leave much to be desire No returns have been received from Japan or the territor it has over-run The declarations of the United Kingdo and the Netherlands to abolish opium smoking in the territories now await effectuation. Argentina, it appear has the distinction of not having ratified any of the narcot drugs conventions, while in the United States, with vigoro organisation, it is claimed that "addiction was reduced as much as 60%"

As regards the future the San Francisco Conference stre the importance of preserving the continuity of the international control of narcotics between the cessation of the League Nations and the institution of the new organisation with economic and social council What the relations of the supe visory body of the League, which establishes the annu estimates of narcotic required for legitimate purposes, a of the Permanent Central Opium Board will be under t new dispensation remains to be seen

Notes and News

CLINIC FOR OLD PEOPLE

In the past year an attempt has been made at Ramsgate to provide a clinic for elderly people, where medical examination and advice would be given on the same terms as they are at infant welfare clinics. In a report reprinted in the *Medical Officer* of Sept 29 (p 103) Dr J V Walker shows that much has already been learned about running such a clinic. On what afterwards proved an error of judgment a more central site than that of the health centre was chosen for the clinic, which was held at 11 o'clock on alternate Tuesdays. No publicity drive was undertaken, but the medical officer of health and the health visitors brought it to the notice of interested people. Attendances were not satisfactory, however, and after six months the clinic was transferred to the health centre, and sessions were held weekly.

It turns out that old people take much longer to examine than babies, and this, Dr Walker feels, may lead authorities who are short of doctors to hesitate about setting up such clinics just at present. Again, wider resources are needed for their care than Ramsgate offers. Many of them are in need of residential care, or are likely to need it though not necessarily in a hospital or public-assistance institution. He suggests that a voluntary agency might be persuaded to establish a home to which the local authority might contribute.

There was also a good deal of overlapping between existing services for the elderly. Some get benefits through the public assistance department, administered in Ramsgate by the Kent county council, and they can also get medical advice from this source but only if they are ill. Dr Walker foresees good opportunities for the health visitors, who visit the old people in their homes and the elderly persons' clinic, to coöperate with the public-assistance medical officer for the benefit of the patient.

LCC AND RELEASED MEDICAL OFFICERS

The Ministry of Health's scheme for postgraduate training of doctors released from the Forces comprises (i) six months' hospital appointments for "young practitioners," (ii) a refresher course for general practitioners; and (iii) courses for trainee specialists. The hospitals and medical services committee of the London County Council proposes that for class i the Council shall create 18 temporary additional positions at £350 a year with resident emoluments or £100 in lieu of them. For class ii it intends to provide at grouped hospitals, four intensive courses running concurrently for a fortnight. From 15 to 20 doctors could attend each course, and, with three courses a year at each group of hospitals, up to 240 general practitioners could be accepted annually. For class iii (trainee specialists) it is offering 11 temporary positions (5 medical and 6 surgical) at £550 a year plus £100 if non resident. This is additional to positions at the Maudsley Hospital mentioned in THE LANCET of Oct 13 (p 483); and it is also additional of course to normal vacancies for resident posts in LCC hospitals. The Council will recover the cost from the Ministry of Health.

NEUROPSYCHIATRIC DISCHARGES FROM UNITED STATES ARMY

Addressing the New York Academy of Medicine on Oct. 8, Brigadier-General William C Menninger said that the number of soldiers discharged from the US Army for neuropsychiatric reasons has now reached 315 000. This fact constituted a post-war challenge to medicine and he hoped that doctors "will prepare themselves to accept and treat what the army medical officers discovered were among their biggest problems—the emotional factors in the production of illness." Discussing the terms "combat exhaustion and combat fatigue" General Menninger said that in only about 3–5% of cases were these states due entirely to fatigue; the condition of the great majority was primarily a personality disturbance. On joining the army a soldier faced an entirely different life which might produce sufficient stress to bring him to the psychiatric breaking point. Frustration was a daily part of this life, sometimes in the form of waiting days, weeks, or months, and sometimes in the deprivation of essential supplies. Confusion was routine in his life "and the noise and whistles and flares of battle are beyond the imagination of anyone who has not heard and seen them." Essentially the response was the same when a person failed to adjust himself to his situation in civilian life.

MARRIAGE AND EMPLOYMENT

Before the war the London County Council made it a rule that women employed in its service should resign on marriage. There were exceptions, including full time doctors "other than in hospital or institutional services," non resident part time doctors and those working on a sessional basis, full time teachers in non residential posts, part time and sessional teachers, various grades of laundry and domestic staff, and women whose husbands were totally incapacitated or who were separated from or had been deserted by their husbands. Early in the war the usual supply of candidates for resident staff ran out and the standing order was temporarily suspended at first for some grades of women staff and finally for all. The general effect has been to allow married women to be employed in all grades for which unmarried women are eligible.

The general purposes committee have now reviewed the whole position considering not only the needs of the service and the Council's obligations but the general principles. With their war experience as a guide they hold that the ban on employment of married women should now be repealed for all grades of staff, and have recommended this step to the Council. Women will of course, still be at liberty to resign on marriage if they wish. Difficulties are foreseen in the case of women in resident posts where there are no married quarters but this the committee hold to be a practical question which can be considered separately.

STUDENTS IN SESSION

The annual general meeting of the British Medical Students' Association begins on Oct. 26 at BMA House, with an address at 3 PM by Lord Moran. Guy's Hospital Students' Union have invited delegates and visitors to a dance in the evening. Business meetings will occupy the morning and afternoon of Oct 27, and Professor Ryle will speak at 4 15 PM on Social Pathology. During the evening a programme of American medical films will be presented. Election of officers will take place on Oct 28 and will be followed by a discussion on plans for the coming year. Inquiries may be made of the BMSA Secretary at BMA House, Tavistock Square, London, WC1.

The first two of the lecture-demonstrations arranged by the British Medical Students' Association for their members in the London region have now taken place. Mr Claud Mullins opened the series with a talk on Medicine and the Magistrate's Courts and many students have since visited his court to see demonstrations of the points he made. Prof E. Hindle gave an address on the Prosectorium of the Zoo and later conducted a party round the Zoological Gardens and the laboratories to demonstrate investigations made into the anatomy, physiology and pathology of animals.

University of Cambridge

On Oct 19 the following degrees were conferred by proxy:

MD, B Chir—J M Cliff, J A R Delenham, F D Forster, R S Lewis, J A Hycroft, J E M Whitehead.

MB—W A Fell.

Royal College of Physicians of London

The subject of Dr John Parkinson's Harveian oration delivered on St. Luke's day, was rheumatic fever and heart disease. The oration will be published in THE LANCET.

On the same day the Moxon medal was awarded to Sir Alexander Fleming, FRS, for his work on penicillin the Weber Parkes prize in absentia to Dr Eugene L. Opie, professor of pathology at Cornell University, for his work on the pathogenesis of pulmonary tuberculosis and the Baly medal to Prof S A S Krogh of the Zoophysiological Laboratory Copenhagen Nobel laureate in physiology and medicine in 1920.

Royal College of Surgeons of England

On Thursday Nov 1 at 5 PM Sir Arthur MacNalty will deliver the Thomas Vicary lecture to the college. He is to speak on the Renaissance—its influence on English medicine surgery, and public health.

Tuberculosis in the Channel Islands

A senior medical officer in the public health department of the London County Council has been lent to the Government "to investigate the large number of cases of tuberculosis reported by the civil authorities in the Channel Islands and to advise on diagnosis and treatment."

Royal College of Physicians of Edinburgh

On Friday, Nov 2, at 4 PM, at the college, 9, Queen Street, Edinburgh, Prof J A Nixon will deliver the Alexander Black lecture He is to speak on the health and safety of the merchant seaman

Royal College of Surgeons of Edinburgh

At a meeting of the college held on Oct 17 the following office-bearers were elected for the ensuing year. president, Mr Jas M Graham, vice president, Prof R W Johnstone, secretary and treasurer, Mr K Paterson Brown, members of president's council, Sir John Fraser, Dr G Ewart Martin, Mr Francis E Jardine, Mr W Quarry Wood, Mr Walter Mercer, Prof J R Learmonth, representative on the General Medical Council, Mr Henry Wade, convener of museum committee, Mr W Quarry Wood, librarian, Dr Douglas Guthrie

The following were admitted to the fellowship

John Boyes LRCPE, A E Bremner, MB ST AND, J A Chalmers, MD EDIN, A W Chambers, LRCPI Prudence Halton, MB LOND, J A Harpman MB LOND, George Hay, MB EDIN, W A N Inglis, MD ALBERTA, E M Innes, MB ABERD, Alberta M Jeans MRCS, Kathleen M Long, MB DURH, R N Martin, MB BELF, Douglas Telford, MD TORONTO, Norman Whalley, MB MANC

Royal Sanitary Institute

A meeting is to be held at the Town Hall, Weston super mare, on Saturday, Nov 3, at 10 15 AM, when Dr C G Eastwood will read a paper entitled David and Goliath—a Plea for the Individual in Social Medicine Dr T L Scott will speak on the control of the movable dwelling

Association of Anæsthetists of Great Britain and Ireland

The annual meeting will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, WC2, on Wednesday, Oct 31, and Thursday, Nov 1 The association's office is at 45, Lincoln's Inn Fields

Research on the Psychology of Tuberculosis

The National Association for the Prevention of Tuberculosis has appointed Major Eric Wittkower, RAMC, to conduct an investigation into the psychology of tuberculosis Major Wittkower will begin this work on his release shortly from military service Before the war Major Wittkower was a Halley-Stewart research fellow and physician at the Tavistock Clinic, London, and for the last five years has been engaged as a psychiatric specialist in the RAMC

Royal Institution of Great Britain

On Thursdays, Nov 1, 8, 15, and 22, at 5 15 PM, Mr James Gray, FRS, professor of zoology in the University of Cambridge, will speak on the anatomy and functions of the brain in lower vertebrates. On Tuesdays, Dec 4, 11, and 18, at 5 15 PM, Sir Henry Dale, OM, FRS, will describe recent developments in chemical therapeutics All the lectures will be held at the institution 21, Albemarle Street, London, W1

Tuberculosis Association

At a meeting to be held at 20, Portland Place, London, W1, on Friday, Nov 16, at 4 45 PM, Prof G S Wilson will speak on bovine infection and disease, and Dr Kalman Mann on the incidence of primary and hæmatogenous lung lesions in skeletal tuberculosis At 8 PM there will be a discussion on prognosis and treatment of combined tuberculosis, when the opening speakers will be Dr Harley Stevens, Mr G R Girdlestone, and Dr. F S Hawkins

Pharmaceutical Society

Dr G A. H Buttle has been appointed professor of pharmacology at the college of the society and has already taken up his chair

Dr Buttle who is 46 was educated at Whitgift School, Croydon, and St John's College, Cambridge He took the Conjoint qualification from University College Hospital in 1924 and obtained his MA Camb three years later After holding an appointment at the London Fever Hospital he joined the team of research workers at Wellcome Physiological Laboratories headed by Parish and Trevan He was early drawn into the pioneer work on the sulphonamides, and in 1936 with Colebrook and O'Meara first described in our columns their mode of action in controlling hæmolytic streptococcal infections Later with colleagues from the Wellcome laboratories he showed that these drugs had a remarkable effect on a variety of experimental infections other than those produced by the *Streptococcus pyogenes* and he investigated the action of many new compounds The outbreak of war altered the direction of Dr Buttle's investigations. He went to Bristol as second in-command of the Army Blood Supply Depot and as officer commanding the base transfusion unit in Egypt he was largely responsible for organising the blood transfusion services of the Middle East Forces Later he did similar work with the 21st Army Group His published work during the war has included papers on blood substitutes in hæmorrhage, on plasma filtration and on the use of diflavine and proflavine in wounds Lieut-Colonel Buttle has recently acted as consultant in blood transfusion to the War Office

Health Services Bill Early Next Year

Addressing the Society of Physiotherapists in London last Saturday, Mr Aneurin Bevan, Minister of Health, said that a Bill providing for a comprehensive health service will be presented to Parliament in the early part of 1946

Royal Society of Medicine

On Thursday, Nov 1, at 8 45 PM, the section of neurology will hold a clinical meeting at the National Hospital, Queen Square, London, WC1 At 10 30 AM, on Nov 2, at 1, Wimpole Street, W1, Mr J A M. Wright will deliver his presidential address to the section of otology on cochlear deafness The section of laryngology will meet at 2 30 PM on the same day to hear Mr Ewart Martin's presidential address on bronchoœsophagy, followed by a discussion, and at 5 30 PM at the section of anæsthetics Dr George Edwards will give his presidential address on tribromethyl alcohol

INFECTIOUS DISEASE IN ENGLAND AND WALES

WEEK ENDED OCT 13

Notifications —The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1849; whooping-cough, 970, diphtheria, 505, paratyphoid, 6, typhoid, 10, measles (excluding rubella), 446, pneumonia (primary or influenzal), 415, puerperal pyrexia, 145, cerebrospinal fever, 36; poliomyelitis, 45; polio-encephalitis, 3; encephalitis lethargica, 1, dysentery, 286, ophthalmia neonatorum, 61 No case of cholera or typhus was notified during the week.

The number of service and civilian sick in the Infectious Hospitals of the London County Council on Oct 10 was 1035. During the previous week the following cases were admitted scarlet fever, 87, diphtheria, 49, measles, 10, whooping-cough, 22

Deaths —In 126 great towns there were no deaths from enteric fever, or measles, 1 (0) from scarlet fever, 3 (1) from whooping-cough, 10 (1) from diphtheria, 50 (5) from diarrhœa and enteritis under two years, and 11 (2) from influenza The figures in parentheses are those for London itself.

The number of stillbirths notified during the week was 206 (corresponding to a rate of 29 per thousand total births), including 26 in London.

Appointments

BLUNT, M J, MB LOND RSO, Peterborough and District Memorial Hospital

DALZIEL, KEITH, B SC LOND graduate assistant in the department of biochemistry, Radcliffe Infirmary, Oxford

RICHARDSON, F C RUTH, MRCS RSO, Children's Hospital, Birmingham

Births, Marriages, and Deaths

BIRTHS

BRAITHWAITE —On Oct 10, at Egremont, Cumberland, the wife of Edward Braithwaite, DM—a son

COXON —On Sept 27, at Adlington, Cheshire, the wife of Captain R V Coxon, RAMC—a daughter

HERTEN GREAVES —On Oct 2, at Buenos Aires, the wife of E C Herten Greaves, FRCS—a daughter

HEYLAND —On Oct 12 at Adlington, Cheshire, the wife of Surgeon Lieutenant Ralph Heyland, RNVR—a son

HOLLINGS —On Oct 12, at Woking, the wife of Lieut Colonel G B. Hollings, RAMC—a daughter

MARRIAGES

BELLAMY—KINNOCH —On Oct 13, at Glasgow, Richard Bellamy, MB, to Margaret Thomson Kinnoch

EDGECOMBE—BUTLER —On Oct 18, at Leeds, Wilfrid Edgecombe, FRCI, FRCS, of Harrogate, to Gabrielle Butler

KEMP—PEACOCK —On Oct. 16, in London, John W L Kemp, MB, to Joyce Peacock

LAIRD—GREEN —On Oct 16, in London, Henry Strachan Laird, captain RAMC, to Kathleen Elspeth Green

DEATHS

BEALE.—On Oct 19, at Folkestone, John Foster Beale, MA CAMB MRCS DPH aged 67

GOODWYN —On Oct 21, Henry Goodwyn, FRCSI, of Newbury Berks, aged 86

JONES —On Sept 24, at Llandudno, David Johnston Jones MD EDIN aged 91

LONGMAN —On Oct 14, Arthur Longman, MRCS of Salisbury, aged 87.

O'HEFFERNAN —On Oct 15 Harold Hilton O'Heffernan, MRCS major, late RAMC, aged 79

SADLER —On Oct 16, at Ashbourne, Derbyshire, Ernest Alfred Sadler, MD LOND aged 81

RAYNER.—On Oct 21, in Bristol, David Charles Rayner, CBE BRIST FRCS FRCOG, aged 80

YOUNG —On Oct 16, at Newcastle, Staffs, Ernest Eric Young MB LOND, FRCS, aged 68

SULPHONAMIDES IN BACILLARY DYSENTERY

FURTHER OBSERVATIONS ON THEIR EFFECTS

J G SCADDING, MD LOND, FRCP
LIEUT-COLONEL RAMC, OFFICER I/C A MEDICAL DIVISION

THE results of observations, made at a large desert general hospital in the Middle East (ME) during the 1943 dysentery season, on the relative efficacy of sulphanilamide, sulphapyridine, and sulphaguanidine in bacillary dysentery have previously been reported (Scadding 1944) It was found that groups of patients treated with these three drugs showed no significant difference in duration of diarrhœa or of stay in hospital. The present paper records the continuation of investigations of sulphonamide treatment in bacillary dysentery during the 1944 season at the same hospital.

Because sulphaguanidine is the standard drug for the treatment of bacillary dysentery in ME, and because it is generally believed that sulphonamides have a specific beneficial effect in this disease, only comparative studies, continuing those carried out in 1943, were made during the earlier part of the season First, succinyl-sulphathiazole and then sulphadiazine were tested against sulphaguanidine. Next, observations without controls were made on the effect of smaller doses of sulphadiazine. Finally, for reasons set out below, it was considered justifiable to carry out a study, scientifically necessary, of strictly alternated sulphaguanidine-treated and control cases The results will be presented in the chronological order in which the observations were made, illogical though it be

MATERIAL AND METHOD

The type of dysentery was similar to that of the previous season. It was mild, as shown by the control untreated cases reported below No acute fulminating case was seen. During each investigation all patients admitted to the dysentery wards with a history of less than five days' diarrhœa and with blood and mucus and a dysenteric exudate in the stools were included in the observed series. The exudate was bacillary—i e , containing more than 50% of polymorphonuclear neutrophils —in 75–80% of cases in all series and indefinite—i.e , containing less than 50% of polymorphonuclear neutrophils—in the rest Facilities for culture were not available until the final control series, the results of stool culture in 99 cases in this series are shown in table IV

Records were kept by which it was hoped to estimate the relative severity of the illness, and the response to treatment They are summarised in the tables. The criteria adopted to estimate *severity* were (1) the duration of diarrhœa before admission, (2) the number of stools in the 24 hr before admission, and (3) the incidence of fever As the highest fever was generally present on admission, it may be included among the criteria of severity The tables show that the severity of the disease, so estimated, remained almost constant throughout the season The slightly lower incidence of fever towards the end of the season (table III and the last column of table II) may be related to the end of the very hot weather

Results of treatment were judged by (1) the duration of fever after admission in febrile cases, (2) the duration of diarrhœa, indicated by the day on which a formed stool was first observed and (3) the total number of days spent in hospital Patients were not discharged until they had passed three formed stools free from blood and mucus In computing for the tables the mean duration of stay in hospital, a few cases in which it was prolonged because of some unrelated disease were omitted Diarrhœa sometimes recurred during convalescence; the incidence in each series is recorded in the tables.

Treatment, besides sulphonamides, consisted of rest in bed ample liquid intake and a bland diet increasing as the patient improved Sulphaguanidine when used was given in a suspension of 3 5 g to 1 oz. of water in doses of 7·0 g followed by 3 5 g four-hourly, reduced after 48 hr if the patient's condition had improved The dosage and form in which the other drugs were given are noted below The average total dose and duration of administration of each drug are recorded in the tables

No complication, renal, gastric, exanthematous, or other, of sulphonamide treatment developed throughout the investigation.

COMPARISON OF RESULTS WITH SUCCINYL-SULPHATHIAZOLE AND WITH SULPHAGUANIDINE

Succinyl-sulphathiazole is even less well absorbed than sulphaguanidine, only 5% of a dose given by mouth being excreted by the kidneys; it remains within the lumen of the bowel and is active there, in normal conditions, against coliform organisms (Poth et al 1942) Hence, on the hypothesis which led originally to the introduction of sulphaguanidine for the treatment of dysentery—i.e , that a sulphonamide which is retained in high concentration in the bowel contents is likely to be effective—succinyl-sulphathiazole would be expected to be better than sulphaguanidine

In June and July, 1944, alternate members of a series of 100 consecutive patients with bacillary dysentery were treated with sulphaguanidine, and the rest with succinyl sulphathiazole The latter drug was given in suspension in water in doses of 2 g five times daily for 3 days, then four times daily for 4 days, the course being cut short if there was early improvement The results are recorded in table I, which shows that the cases in the two groups were of similar severity that the durations of fever and of diarrhœa were very similar, and that the only difference is that the sulphaguanidine treated patients were in hospital, on the average, 1 3 days longer than those treated with succinyl-sulphathiazole, and showed a greater tendency to recurrence of diarrhœa during convalescence

COMPARISON OF RESULTS WITH SULPHADIAZINE AND WITH SULPHAGUANIDINE

Sulphadiazine presents a complete contrast to succinyl sulphathiazole in being readily absorbed Hardy and Watt (1944a) state that bacillary dysentery responds earlier to sulphadiazine and other well-absorbed sulphonamides than to poorly absorbed sulphonamides

In August and September, 1944, alternate members of a series of 100 consecutive patients were treated with sulphaguanidine, and the rest with sulphadiazine The latter drug was given in 0 5 g tablets in doses of 1·0 g *five times daily, reduced after 48 hr, if there was* improvement, to thrice daily The results are recorded in table II, which shows that the cases in the two groups are comparable in severity Those treated with sulphadiazine had, on the average, slightly shorter fever and very slightly shorter duration of diarrhœa and of stay in hospital

OBSERVATIONS ON TREATMENT WITH SMALLER DOSES OF SULPHADIAZINE WITHOUT CONTROLS

In September and October, 1944, the effect of reducing the dosage of sulphadiazine was observed without controls. At first 4 g daily and then 3 g daily was given The results were very little different from those obtained with 5 g daily; those obtained in 57 cases treated with 3 g daily (average dose 11·4 g in 4 days) are recorded in table II which shows that, comparing this group with the others summarised in the same table, though the series was not directly controlled the severity of the cases was similar, except that the incidence of fever was slightly less, the fever and the diarrhœa very slightly longer, and the stay in hospital rather shorter than in the series treated with larger doses.

CONCURRENT SERIES OF SULPHAGUANIDINE TREATED AND CONTROL UNTREATED CASES

In discussing the 1943 observations at this hospital I remarked that a possible conclusion was that, in the mild type of dysentery treated, none of the three drugs—i e , sulphanilamide sulphapyridine, and sulphaguanidine—had any specific effect, though clinical impressions and the published experience of others were against this view (Scadding 1944) The uniformity of the course of the disease in both the present and the 1943 series of investigations in cases receiving varying dosages and various sulphonamides, both readily and poorly absorbable brought this opinion very forcibly to mind and made it clearly necessary to test the hypothesis that under the conditions of the investigation and by the criteria adopted, no effect of the sulphonamides tested on the clinical course of the type of dysentery treated was detectable

Accordingly a series of strictly alternated sulphaguanidine-treated and control cases was arranged. The controls received a suspension of gr. 20 (1.3 g.) of calcium carbonate to the ounce, which was given in the same volume-dosage and frequency as the suspension of sulphaguanidine. This control suspension was chosen because it closely resembles one of sulphaguanidine, and because it can reasonably be supposed that such a small dose of such an inert substance can have no appreciable effect on the course of the disease. To avoid the danger of leaving a seriously ill patient untreated with a possibly beneficial drug, advantage was taken of the fact that it had been shown that sulphadiazine is at least as effective as sulphaguanidine, and it was ruled that any patient on either suspension about whom any anxiety was felt should cease taking the suspension and be given sulphadiazine.

Soon after this series was started it became possible to perform routine stool-cultures. These were done in 99 of the 133 cases. During 10 days of the total period the overheating of an incubator seriously reduced the number of isolations; this affected the results of about a third of the cultures performed. Nevertheless, there were 45 isolations, distributed among the various bacterial types as shown in table IV. The distribution is very similar to that observed in ME in 8665 cases by Fairley and Boyd (1943). It will be noted that the bacterial types are almost evenly distributed between the treated and the control groups.

Table III sets out the results obtained in this strictly controlled series. Further, the figures for the cases in which an organism of the Flexner group was isolated from the stool are set out separately; there were 17 of these in the treated and 17 in the control group.

The table shows that the cases in the two groups were of comparable severity. The control group of 67 patients had formed stools in a mean time of 5.0 days after admission, remained in hospital for a mean time of 12.3 days, and those who were febrile remained so for a mean time of 2–3 days after admission; whereas the corresponding figures for 66 patients treated with a mean dose of 72 g. of sulphaguanidine in 4–6 days were 4.4, 10.8, and 1.7 days. One patient in each group was thought to be making such unsatisfactory progress that the suspension was changed to sulphadiazine 1.0 g. four times daily; in both improvement followed, but clearly the significance of this event is doubtful.

The figures for duration of diarrhœa and of stay in hospital have been analysed statistically, with the following results:

(1) *Duration of diarrhœa*

Treated cases: mean (days) 4.4, standard deviation 1.3
Control cases: mean (days) 5.0, standard deviation 2.6
Difference of means 0.6
Standard error of difference of means 0.36

(2) *Duration of stay in hospital*

Treated cases: mean (days) 10.8, standard deviation 6.6
Control cases: mean (days) 12.3, standard deviation 7.7
Difference of means 1.5
Standard error of difference of means 1.25.

In both instances the difference of the means, being considerably less than twice its standard error, is not statistically significant.

In the 34 proved Flexner cases the difference between the 17 treated and the 17 controls was even less; if allowance is made for the fact that the average duration before admission in the treated cases was half a day longer than in the controls, there is nothing to suggest that sulphaguanidine had any influence whatever on the course of the disease; the mean total duration of diarrhœa from the onset (not from admission) is 7.0 days in both groups, and the total duration from onset to discharge from hospital is 12.5 days in both groups.

An interesting point is that the control suspension, which was given in the same way as the sulphaguanidine suspension, was found to have been administered in almost exactly the same total volume-dosage and for the same period as the sulphaguanidine. For instance, in the Flexner cases the average total dosage of both sulphaguanidine and control suspensions was 21 oz. in 4 days.

It is possible that in the figures for all cases a beneficial effect on a few severe infections was being masked by dilution with a large number of mild self-terminating

Consideration of the small number of Shiga cases d[illegible] some support to this hypothesis, although obviously no conclusion can be drawn from only 6 cases. The 3 in the control series had formed stools in 12, 11, and 18 days, and were in hospital 21, 30, and 34 days, and the last of these was the one case in the control series which eventually received sulphadiazine; whereas the 3 in the sulphaguanidine-treated series had formed stools in 5, 7, and 7 days, and remained in hospital 9, 26, and 12 days. But the severity of the control cases on admission was greater; their average number of stools in 24 hr. before admission was 22 and their average temperature on admission 101.4° F., whereas the corresponding figures for the treated cases were 15 and 99.3° F. Thus no definite conclusion can be drawn, especially as very great variations in the severity of Shiga infections have been observed in this area, though the evidence seems very suggestive that in this type of case the sulphonamides were beneficial. In this connexion it is interesting to note that Gard (1943) regarded a duration of diarrhœa for an average of 11.5 days in 25 sulphaguanidine-treated cases of Shiga dysentery as a good result of treatment.

DISCUSSION

Many favourable reports on the action of sulphonamides in bacillary dysentery have been published, but few with adequate controls. Good results in uncontrolled series of cases treated with sulphaguanidine have been claimed by Marshall et al. (1941), Lyon (1941, 1942), Fairley and Boyd (1942), Brewer (1943), Bulmer and Priest (1943), Gard (1943), and others. Similar results in more or less controlled series have been reported by Anderson and Cruickshank (1941), who used extremely small doses the activity of which may well be doubted, Clay (1943), and Adams and Atwood (1944). Jamieson et al. (1944) found in a series of not as a rule severe infections, 75% with Flexner strains and 20% with Sonne, that stools were normal in 100 patients treated with sulphaguanidine in an average of 5.0 days, in 50 treated with chalk in 6.0 days, and in 50 treated with aperients in 6.5 days.

Succinyl-sulphathiazole has been reported on favourably in uncontrolled observations by Poth et al. (1942), and Lyon (1943). On the other hand, Roberts and Daniels (1943) report an outbreak of mild dysentery due to a Flexner strain in which 89 patients treated with succinyl-sulphathiazole were compared with 136 untreated controls; no significant difference in degree or duration of diarrhœa or in amelioration of symptoms was noted, though there was a reduction in the convalescent carrier-rate.

The absorbable sulphonamides have been considered efficacious in uncontrolled observations by many workers: for instance, sulphapyridine by Reitler and Marberg (1941), Masefield (1941), Paulley (1942), and Swyer (1943), and sulphathiazole by Ferriman and Mackenzie (1944).

Hardy and Watt (1944a) have studied the effects of three poorly absorbed compounds, sulphaguanidine, succinyl-sulphathiazole, and phthalyl-sulphathiazole, and of five well-absorbed compounds, sulphathiazole, sulphadiazine, sulphamethazine, sulphamerazine, and sulphapyrazine, and state that it was evident, through a comparison with findings in untreated controls, that all these sulphonamides were beneficial in patients with "shigellosis", the only two of their publications (Hardy and Watt 1944a and b) to which I have had access do not quote their actual data.

Observers who have reported on Sonne infections agree that these are little, if at all, affected by any sulphonamide except possibly succinyl-sulphathiazole (Hardy and Watt 1944b, Fairbrother 1944, Adams and Atwood 1944).

Scott (1945) has assessed the value of sulphaguanidine treatment in ME by comparing the duration of stay in hospital of patients with bacillary dysentery in 194[illegible] before, and in 1943 after, the use of sulphaguanidine became general. He found that the mean duration of stay in hospital in 1940 was 12.7 days and in 1943 was 11.6, the difference is statistically significant, but he considers that the discontinuance of routine purgation is a possible contributory factor in this reduction.

Although the data presented in this paper have no relevance to the efficacy of sulphonamides in controlling the carrier state after bacillary dysentery, it is of interest to note that even on this topic reports are conflicting

TABLE I—CONCURRENT SERIES OF CASES TREATED WITH SUCCINYL-SULPHATHIAZOLE AND OF CASES TREATED WITH SULPHAGUANIDINE (JUNE–JULY 1944)

TABLE II—CONCURRENT SERIES OF CASES TREATED WITH SULPHADIAZINE 5 G. DAILY AND OF CASES TREATED WITH SULPHAGUANIDINE (AUGUST–SEPTEMBER 1944), AND UNCONTROLLED SERIES TREATED WITH SULPHADIAZINE 3 G. DAILY (SEPTEMBER–OCTOBER, 1944)

TABLE III—CONCURRENT SERIES OF SULPHAGUANIDINE TREATED AND CONTROL CASES (OCTOBER–NOVEMBER, 1944)

	I		II			III			
			Concurrent		Uncontrolled	All cases		Proved Flexner cases only	
	Succinyl sulphathiazole*	Sulphaguanidine*	Sulphadiazine (5 g. daily)	Sulphaguanidine	Sulphadiazine (3 g. daily)	Sulphaguanidine	Control	Sulphaguanidine	Control
Total no. of cases	50	50	50	50	57	66	67	17	17
Severity									
Mean duration before admission (days)	3·1	2·1	2·1	2·3	2·5	2·8	2·6	3·0	2·5
Mean no. of stools in day before admission	13·0	12·7	12·2	11·5	12·2	13	13	13	12
Fever: percentage febrile	80%	86%	80%	84%	65%	58%	61%	65%	59%
Mean maximum recorded in febrile cases	99·8° F.	100·1° F.	100·4° F.	100·0° F.	100·4° F.	100·4° F.	100·8° F.	100·2° F.	101·4° F.
Results									
Mean duration of fever in febrile cases (days)	1·6	1·7	1·3	1·6	1·4	1·7	2·3	1·6	2·3
Mean duration of diarrhœa after admission (days)	3·5	3·4	3·9	4·3	4·3	4·4	5·0	4·0	4·5
Mean stay in hospital (days)	10·2	11·0	11·6	12·3	10·5	10·8†	10·3†	9·5‡	13·0
Recurrent diarrhœa during convalescence	nil	3 cases	1 case	2 cases	1 case	3 cases	nil	1 case	nil
Dosage (grammes)									
Minimum	11	31·5	8	30	5	31·5		31·5	
Maximum	51	113·5	27	112	22	129·5		126·0	
Mean	38	80·5	17·4	60	11·4	72·0		74·0	
Duration of treatment (days)									
Minimum	2	2	2	2	2	3		3	
Maximum	5	8	7	8	7	9		9	
Mean			4·3	4·0	4·0	4·6		4·0	
Further treatment with sulphadiazine						1 case	1 case	nil	nil

* 4 cases in the succinyl sulphathiazole and 1 in the sulphaguanidine series in which the stay in hospital was extended because of another disease were omitted in calculating these figures.

† In computing these figures, 1 patient in the treated and 2 in the control group whose stay in hospital was prolonged because of unrelated conditions are omitted.

‡ In computing this figure 1 patient who remained in hospital for 40 days because of recurrent diarrhœa is omitted as it introduces a large bias into such a small series. If this case is included the figure for mean stay in hospital for treated Flexner cases increases to 11·4.

Hoagland et al. (1943) report uniformly good results in the treatment of carriers of *Shigella paradysenteriæ* (Flexner and allied strains) with sulphaguanidine and succinyl-sulphathiazole; Barker (1943) had some difficulty in controlling Flexner carriers with succinyl sulphathiazole; Fairbrother (1944) speaks with some reserve of the results of attempts to clear carriers of dysentery bacilli with sulphaguanidine if stringent tests of clearance are applied; while Sandweiss (1944), comparing 33 carriers treated with phthalyl sulphathiazole with 30 untreated carriers, states that the drug did not appear to influence the carrier state, and that in fact a higher proportion of his treated cases continued as carriers.

Thus, there is still no agreement about the value of sulphonamides in dysentery. And the interpretation of the data here presented is difficult. The following statements seem permissible:

(1) In a mixed group of dysenteries, presumably due to several strains of bacilli, sulphaguanidine-treated cases showed a slight advantage over controls in mean duration of diarrhœa and of stay in hospital, but the differences were not statistically significant. It may be that an effect on a few more severe cases was being masked by dilution with a large number of mild self-terminating cases, because (a) in a group of 74 mild Flexner infections, equally divided between the treated and control series, no clinical effect of sulphaguanidine could be demonstrated, and (b) in 6 Shiga infections there was very suggestive evidence that sulphaguanidine and sulphadiazine were beneficial, though the small number of cases observed permits no definite conclusion.

TABLE IV—BACILLARY TYPES ISOLATED IN 99 CASES OF THE SERIES SUMMARISED IN TABLE III

—	Total	Sulphaguanidine treated	Control
No. of cases in which stools were cultured	99	44	45
Isolations			
Total	45	22	23
Flexner	34 (75·6%)	17	1
Shiga	6 (13·3%)	5	3
Para-shiga	1 (2·2%)		1
Sonne	2 (4·4%)	2	
Schmitz	2 (4·4%)		2

The figures in parentheses indicate the percentage of the total isolations constituted by each bacterial type.

(2) In a similar mixed group of dysenteries comparative observations between sulphaguanidine and succinyl-sulphathiazole, and between sulphaguanidine and sulphadiazine, showed differences in mean duration of fever, of diarrhœa, and of stay in hospital smaller than those between the sulphaguanidine-treated and untreated control groups Such as they are, they favour sulphadiazine, and to a less extent succinyl-sulphathiazole, over sulphaguanidine; and this applies even when dosage of sulphadiazine is reduced to 3 g daily.

A difference of the same order in favour of two soluble sulphonamides, sulphapyridine and sulphanilamide, was found in the 1943 observations (Scadding 1944) Though the evidence presented is not conclusively in favour of any sulphonamide, it favours, if any, the readily absorbable more than the poorly absorbable ones

SULPHADIAZINE IN CHRONIC BACILLARY DYSENTERY

Where statistical evidence is so equivocal, it is perhaps permissible, even though dangerous, to mention clinical impressions I have been impressed by a number of cases in which sulphadiazine has seemed to cut short a long-continued bacillary-type dysentery on which the poorly absorbed sulphonamides had had no effect. The following brief case-records illustrate this point.

CASE 1 —A man, aged 44, was admitted with a history of intermittent diarrhœa with blood and mucus for 2 months Microscopy of the stool showed bacillary exudate, from a culture at a later date no pathogens were isolated, many examinations were negative for *Entamœba histolytica* He received a course of 150 g of sulphaguanidine in 8 days without effect, 23 days after admission he was still passing 3 stools daily with blood and mucus

Sigmoidoscopy showed gross thickening and redness of the mucosa, with many submucous hæmorrhages, and much mucopus. He then received 62 g of succinyl-suphathiazole in 7 days, no definite benefit followed this, and 55 days after admission a second sigmoidoscopy showed no appreciable change in the appearances He was then given sulphadiazine 5 g daily for 7 days Immediate improvement followed; the stools were reduced to 1 or 2 daily, usually with mucus Sigmoidoscopy 80 days after admission showed only slight thickening and hyperæmia of the mucosa He was discharged to convalescent depot 86 days after admission, the stools then being normal, once daily, with only occasionally a little mucus The condition has subsequently relapsed and once more responded to sulphadiazine

CASE 2 —An officer, aged 29, was admitted with a history of 14 days' diarrhœa, 5–6 times daily, with blood and mucus Sulphaguanidine given in the usual doses for 4 days had no effect *Sigmoidoscopy* after this showed general thickening and redness of the mucosa up to 3 in., but above this was normal He was still passing loose stools with some blood and mucus 26 days after admission, and an indefinite exudate was found microscopically From the 27th to 35th day he received sulphadiazine 5 g daily, after the second day of this treatment the stools became normal and remained so until he was discharged fit on the 43rd day after admission

In the following case a patient with bacillary dysentery developed arthritis while receiving sulphaguanidine, and both the dysentery and the arthritis responded well to sulphadiazine

CASE 3 —A man, aged 23, was admitted with a history of 3 days' diarrhœa with blood and mucus, 25 stools in 24 hr before admission Microscopy of the stool showed indefinite exudate Sulphaguanidine was started in the usual doses On the 3rd day of treatment with sulphaguanidine the right knee became swollen and painful, and temperature rose to 100° F. On the following day the other knee was swollen, temperature 100 6° F, and 10 stools with blood and mucus had been passed in 24 hr in spite of continued sulphaguanidine treatment This was stopped after 73 g had been given, and sulphadiazine 5 g daily was substituted Improvement followed immediately The next day the temperature was normal, the stools steadily diminished in number until on the 8th day of sulphadiazine treatment they were normal, and the arthritis rapidly subsided. He received 30 g of sulphadiazine in all and was discharged fit 21 days after admission

It is a plausible hypothesis that in these chronic cases the mode of action of sulphonamides is to combat invasion of the bowel wall by secondary invaders, by virtue of their concentration in the blood, rather than on the dysentery bacilli by their concentration in the lumen of the bowel, where there are likely to be inhibitory substances, certainly in severe cases there is an inhibitory substance—i.e, pus—in the lumen of the bowel If this be true, it explains the superiority of the soluble sulphonamides Also, on the hypothesis that the mode of action of sulphonamides in acute cases is simply prophylactic against ulceration, either by the action of the dysentery organisms or by secondary invaders, it is easy to explain (1) the difficulty of detecting any effect in groups of mild cases, in which no ulceration is likely to develop in any event, (2) the irregular response in severe cases, since response will depend on what secondary invaders are prominent in any given case, and (3) the fact that small doses of readily absorbable sulphonamides, which for other infections would be regarded as prophylactic rather than therapeutic, give as good results in acute bacillary dysentery as larger ones, and possibly better results than very much larger doses of the poorly absorbable compounds.

Estimations of the sulphonamide content of the blood were not possible in the reported series, but it seems likely that the blood sulphonamide content produced by giving 21 g daily of sulphaguanidine, of which it is known that over 50% may be excreted in the urine, is not very different from that produced by the small doses (3–5 g. daily) of sulphadiazine On the hypothesis advanced above it would be expected that penicillin parenterally would be as effective as or more effective than either poorly or well absorbed sulphonamides in bacillary dysentery A trial of penicillin, especially in severe cases, seems well worth while; though, as has been shown, the simplest of treatment suffices for the ordinary mild case.

CONCLUSIONS

The only definite conclusions that can be drawn from these and my previous observations (Scadding 1944) is that the absorbable sulphonamides, even in small doses, were at least as effective as, and possibly more effective than, the poorly absorbable sulphonamides in the treatment of bacillary dysentery of the type at present seen in ME On the question of the effectiveness of the sulphonamides in general, no statistically satisfactory evidence was obtained, though the clinical impression that severe and some chronic cases benefited, especially from moderate doses of sulphadiazine, was strong The observations were relevant only to the therapy of the individual case; the important question of the effect of sulphonamides on the carrier state was not investigated

SUMMARY

The therapeutic effects of sulphaguanidine, succinyl sulphathiazole, and sulphadiazine have been investigated in observations on 390 unselected cases of acute bacillary dysentery.

The disease was on the whole of a mild type A series of 67 control cases were treated by rest and diet only, except 1 with a Shiga infection whose progress was so poor that sulphadiazine was given The mean duration of diarrhœa in this group was 5 0 days and of stay in hospital 12 3 days The corresponding figures for 66 alternate cases treated with sulphaguanidine were 4·4 and 10 8 days; and in this group also 1 case made such slow progress that additional treatment with sulphadiazine was given The differences between treated and untreated groups are not statistically significant.

Of 34 Flexner cases 17 were in the sulphaguanidine-treated and 17 in the control group; there was no difference in the course of the disease in the two groups.

In 6 Shiga cases there was suggestive evidence that sulphonamide treatment had proved beneficial

In comparative studies of succinyl-sulphathiazole and sulphaguanidine, and of sulphadiazine and sulphaguanidine, the differences in results were small, sulphadiazine, even in doses as small as 3 g daily, gave results very slightly better than those given by sulphaguanidine

Good results are reported in the treatment of a few cases of chronic bacillary dysentery with sulphadiazine

A hypothesis is advanced to account for the observation that prophylactic doses of absorbable sulphonamides are at least as effective as large doses of either readily or poorly absorbable sulphonamides.

ADDENDUM

Since this paper was written a United States War Department Technical Bulletin (1944) has come to hand, recommending sulphadiazine in doses of 2 g initially, followed by 1 g four times a day, as the drug of choice in the treatment of bacillary dysentery

I am indebted to the sisters and medical officers at various times in charge of the dysentery wards for their coöperation, without which this work could not have been done; to Major L. G Cook for the stool cultures; and to Lieut.-Colonel R. B Scott for help with the statistical analysis

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EFFECTS OF ARTIFICIAL DEHYDRATION IN RHEUMATISM

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The clinical effect of altering the volume and distribution of the body fluids has been studied at a general hospital in cases of fibrositis, acute and subacute articular rheumatism, and sciatica.

FIBROSITIS

It is now generally accepted that the pain in true fibrositis is associated with circumscribed areas of local tenderness usually called trigger points, and that the symptoms can often be relieved, sometimes permanently, by injection of procaine into those areas

These trigger points may be palpable as small tender nodules, especially where they can be compressed against bone Painless nodules in these regions, however, do not seem to signify rheumatism In a recent examination of 500 soldiers non tender nodules were found equally frequently in fibrositic and non fibrositic subjects, but tender nodules and trigger points were found in only 3% of men who did not give a clear history of fibrositis as compared with 30% in those who did

Stockman (1920) believed these tender nodules to be foci of inflammatory reaction situated in the deep fibrous tissues or in the muscles (fibromyositis) Lilliott (1944) has demonstrated areas of local muscle spasm in various conditions associated with deep pain and tenderness, and has suggested that the pain in fibrositis as well as the trigger points can be explained on this basis Although we consider that muscle spasm can contribute to the pain and tenderness, we regard it as being a reflex response to irritation from a pathological process situated in tissues outside the muscles.

It has been shown that trigger points occur with great regularity in certain regions of the body, and that these regions coincide with the distribution of basic fatty tissue which persists even in emaciated bodies (Copeman and Ackerman 1941) In the lumbar region pads of fatty tissue overlie the lateral borders of the paravertebral muscles and may be 2 in. thick This is a common situation for trigger points, and location of these by needling has shown that they are too superficial to be lying in the muscles In the upper back and shoulders the layer of fatty tissue is thinner, and tender nodules can often be picked up with the subcutaneous tissues between the examiner s finger and thumb Dissection of these areas of fatty tissue shows that they consist of lobules of fat lying within definite compartments with tough fibrous walls. The lobules do not appear normally to fill the space available within the compartments.

We believe that in fibrositis an important factor in the production of pain and local tenderness is œdema in certain lobules and the development of tension as they swell and fill their compartments This increase in size may lead to herniation if the fascial walls are partially deficient In 20 cases of established fibrositis such fat herniæ were demonstrated at biopsy, and their removal was followed by persistent relief of symptoms On microscopical examination of the biopsy material no histological evidence of inflammation was found in the form of cellular infiltration, although macroscopically there was obvious œdema and congestion; therefore the swelling must have resulted from some process other than the classical inflammatory reaction

We thought that we might be able to reverse this process by reduction of the fluid-content of the affected tissues, probably by inducing the clinical state of dehydration. This study was chiefly concerned with cases of fibrositis of the back and shoulders, but many other cases were seen in which other parts of the body were affected These latter cases showed the same tendency to recurrence and exacerbation in response to infection and climatic influences, and trigger points were found in constant situations corresponding to the distribution of fibro-fatty tissue round tendon sheaths, bursæ and muscle insertions. It seemed therefore that a similar process of œdema and tension affecting fibro-fatty tissue might be responsible for the symptoms in this type of case also; accordingly they are included separately as chronic rheumatism in the accompanying table

ACUTE AND SUBACUTE ARTICULAR RHEUMATISM

Most cases of acute rheumatism were of a benign type and of comparatively short duration. In some cases however, articular pains started to recur in wet weather; whereas others merged into a condition clinically indistinguishable from chronic fibrositis. We repeatedly observed that the articular pain in acute and subacute rheumatism was referred from one or more trigger points near the joint and was not caused as is generally assumed, by distension of the joint through effusion, which often only happens later in the disease This can be confirmed by infiltrating these trigger points with procaine, which immediately relieves the so-called articular pain without affecting the effusion. Moreover, tense swollen joints are seen in painless conditions such as hydarthrosis and synovitis

These observations show that the distinction between acute and subacute rheumatism and fibrositis is not so precise as is generally held, there being many points of resemblance between them In view of these facts some cases of acute and of subacute articular rheumatism were also submitted to dehydration

SCIATICA

In planning this experiment it was thought that cases of sciatica due to a prolapse of an intervertebral disk might prove suitable for a control series. The effect of dehydration was therefore tried on several cases and it was found that, contrary to expectation, they tended to respond to the procedure in a characteristic manner, different from that seen in fibrositis.

FATTY TISSUE AND WATER METABOLISM

The fatty tissues have long been known to be connected in some way with the normal water storage of the body although not much information appears yet to be available on this subject, except as it affects the hump of the camel.

Chiari (1910) has said that adipose tissue constitutes 18% of the weight of normal persons and is subject to many physiological and pathological variations, although

no textbook refers to it as a system subject to its own diseases. Wells (1940) has pointed out that it seems never to have been considered that these tissues might play a part in systemic disease

Wassermann (1931) and Wells (1940) have found that the thin ring of cytoplasm of the distended fat-cell can swell with fluids, and that the depleted fat-cell will also take up water and become hydropic, thus playing a direct part in water metabolism This conception is reinforced by the remarkable and deceptive water losses and retentions observed in the course of treatment of the obese.

To regulate the functional activity of the fat-tissue there is an abundant sympathetic nerve-supply both to the blood-vessels and the parenchyma; and Becke (1933) has demonstrated fibres running to individual fat-cells. Section of these nerves modifies the behaviour of the fat-cells in storage and in yielding, and no doubt also in other directions It is probable that pain fibres also run with these nerves, since lipomata may become extremely painful Lyon (1910) stated that nerves examined from nodular lipomatous areas and areas of generalised painful adiposity showed interstitial neuritis in the region of the deposits.

DEHYDRATION

Water constitutes 70% of the body-weight, and the portion contained within the cells, including the blood corpuscles, is known as intracellular fluid The rest is shared between the blood-vessels and the tissue spaces as plasma and interstitial fluid and is referred to collectively as extracellular fluid The distribution of fluids in a man of 60 kg. body-weight is approximately as follows ·

	% of body-weight	Volume (litres)
Intracellular fluid	50	30
Extracellular fluid	20	12
Interstitial fluid	15	9
Plasma	5	3

Dehydration may be defined as reduction of the volume of the body fluids, and it is convenient to distinguish three types, extracellular, intracellular, and general dehydration.

Extracellular Dehydration.—This is caused by reduction in the total quantity of electrolytes present in extracellular fluid Sodium forms 90% of the cation and chlorine 70% of the anion; neither of these ions is present in the cells, nor is the cell membrane permeable to them When the content of sodium and chloride is reduced, the kidney correspondingly reduces the body fluids to maintain their total electrolyte concentration and osmotic value

Unlike other forms of dehydration, this type does not cause thirst (Dill 1936), and, in the absence of an intake of salt sufficient to make good the deficiency, it is unrelieved by taking fluids, as they cannot be retained by the body This condition is seen clinically in heat exhaustion, dysentery, and intestinal obstruction. Plasma volume and circulatory efficiency are not seriously affected until a quantity of fluid equivalent to 6% of the weight of the body has been lost

Therapeutically, extracellular dehydration may be induced by the promotion of sweating Salt-free diets are often ordered for this purpose, but in the absence of sweating they are probably of little effect in reducing body water, since the kidney conserves electrolyte by checking the output of sodium and chloride in the urine.

Intracellular Dehydration—This may be induced by the intravenous injection of sodium chloride, provided that fluids are concurrently withheld, and this is one of the methods used by us The addition of electrolyte to the extracellular fluid raises its osmotic pressure, and, since the cell membrane is impermeable to sodium and chloride ions (Gamble 1942), water is withdrawn from the tissues to an extent sufficient to restore the disturbed osmotic equilibrium between the cells and their environment

An important though transient effect of intravenous injections of hypertonic saline is the rapid transfer of extracellular water from the tissue spaces to the blood-vessels, with a consequent and temporary increase in blood volume Although the capillary membrane is readily permeable to sodium and chloride, osmotic effects take place while diffusion is proceeding. In the central nervous system there is an extensive fall of cerebrospinal-fluid pressure which is said to last 2-4 hours or even longer and to be accompanied by pronounced shrinking of the nervous tissue (Wright 1940). We believe that such an effect may explain the relief of symptoms noted by us in sciatica due to pressure on a nerve-root by a prolapsed intervertebral disk.

General Dehydration.—This is induced by abstention from drinking and not essentially by loss of electrolyte or disturbance of osmotic equilibrium. Continued loss of water through the skin, lungs, and kidneys causes a progressive fall in body-weight at a rate determined by such factors as bodily activity, climatic conditions, and food consumption. Fluid reduction equivalent to 1-2% of body-weight a day is readily tolerated for 3-4 days, and the blood volume is well maintained and shows little change even after a loss of 8½ litres of water (Black et al 1944).

By measurement of changes in the total output of sodium and potassium in the urine during the period of dehydration it has been shown that the water loss is shared proportionately between the extra- and intracellular fluid—i.e, in the ratio of 1 3 (Black 1945) The addition of sodium and chloride to the extracellular fluid under these conditions accentuates the rise of osmotic pressure of the body fluids, increases the output of urine, and adds to the general effect of intracellular dehydration

With regard to other possible methods of inducing general dehydration, such as the use of diuretics and purgatives, the effect on the total quantity and distribution of body water might be expected to be determined by the relative loss of electrolyte and water and would depend on the principles described above. Purgation with large doses of sodium sulphate was used by us as an adjunct to fluid restriction, and in this case rough estimation of the concentration of chloride and bicarbonate in the stools provided evidence that the loss of electrolyte from the body was small in relation to the volume of fluid withdrawn

METHOD OF DEHYDRATION

In the first 15 patients intake of fluid was restricted for four days to about 8 oz. (225 c cm) daily, dry food being allowed Owing to the difficulty of controlling the patients, however, and the discomfort caused by so long a period of restriction, it was decided to shorten the treatment to 24 hours. During this period neither food nor drink was taken, and fluid output was increased by the administration of sodium sulphate ½ oz. at hourly intervals for 6 doses The quantity of fæces passed was 0 5-4 0 litres (average 1 6 litres) and of urine 40-560 c cm in the 24 hours

As the results obtained by the second method appeared to be less satisfactory, the period of fluid restriction was raised to 36 hours, which remained our standard practice for the last 40 cases At this point a weighing-machine became available, and the progress of dehydration could be followed by measurement of body-weight Loss of weight was found to vary considerably, ranging from 1 to 3 5 kg.; recovery took 2-3 days.

It is recognised that variation in the efficiency of this preliminary period of dehydration influenced the results obtained, but, as the differences between the groups were less than within the groups, the separate analysis for each modification is omitted

In all cases this preliminary dehydration was followed by an intravenous injection of 50 c cm. of 30% sodium chloride (15 g) into one of the veins of the arm At first the injection was made slowly over a period of 15 min, but this was followed by intense pain and in some cases thrombophlebitis extending up the arm for several inches It was later found that, if the injection was made rapidly and leakage round the vein avoided, pain did not arise Localised thrombosis still developed in about half of the cases but passed off in a few days

Immediately after the injection the patient was allowed to drink 4 oz of tea to mitigate thirst. Apart from this no fluid was permitted for 4 hours, after which time no further restriction was imposed, and the patient was encouraged to get up and about

PHYSIOLOGICAL EFFECTS

The general effects resulting from this rapid method of injection were as follows

(1) Transient rise of the pulse-rate by 5–15 beats per min.; followed by a fall within 15 min. to 4–12 beats below the original rate.
(2) Flushing of the face, and a sensation of heat involving the whole body, and usually accompanied by giddiness; these effects passed off within 5 min.
(3) In some cases a salt taste developed in the mouth within 10–30 sec. of the start of the injection.
(4) In all cases the injection was followed by an intensification of the sensation of thirst induced by the preliminary dehydration.

CLINICAL EFFECTS

The application of dehydration to the rheumatic diseases was planned as a physiological experiment to test the hypotheses mentioned above. It was not anticipated that any relief of pain which might result would be anything but temporary. As, however, certain patients were apparently cured by this procedure, our cases have been analysed in such a manner that the potential therapeutic value of dehydration may be demonstrated. For this reason we have been conservative in our assessment, no result which fell short of 75% improvement being claimed as successful. The criteria of success were increase in functional activity, estimated by the performance of certain movements and exercises on initial examination and on discharge; and the relief of pain.

Dehydration was used in 22 cases of typical fibrositis in the acute, subacute, and chronic stages. Of these, 18 were graded as successful and 6 as failures. These cases, as mentioned above, were mostly affected in the back and shoulders and conformed to a fairly standardised clinical picture.

A less standardised group of patients with generalised fibrositis, some of whom had a history of previous mild articular pains and a temporary rise in the erythrocyte sedimentation rate (ESR), has been discussed and labelled Chronic rheumatism. *The response of this group to dehydration was, on the whole, good (see table).* If these results are added to those in typical

RESULTS OF DEHYDRATION IN SCIATICA, FIBROSITIS, AND "CHRONIC RHEUMATISM".

Result	Sciatica	Fibrositis	Chronic rheumatism	Fibrositis and chronic rheumatism combined	Total
Success	11	13	13	26 (63%)	37
Failure	17	9	6	15 (37%)	32
	28	22	19	41	69

Success = 75% relief (maintained) and over

fibrositis and then compared with those in sciatica (in which a different mechanism is probably operative), the success ratio is about 3:1 in fibrositis and chronic rheumatism and is about 3:2 in sciatica, if all transient results are omitted. This difference is statistically significant ($\chi^2 = 3.89$, $P < 0.05$).

We also dehydrated 28 patients with sciatica and neurological evidence of prolapse of an intervertebral disk. Contrary to expectation, pain also yielded in rapid and characteristic fashion in more than half, although usually only temporarily. Where this was 100% successful, the full effect was achieved within 10 min. of the final saline injection and lasted 1–6 hours. After this the pain either returned fairly rapidly or else redeveloped gradually during the next 4–5 days, not always in its former intensity. In 3 cases the pain did not return, and the men left hospital apparently cured.

We consider that the mechanism of relief of pain in sciatica differs from that in fibrositis and rheumatism and is probably the effect of shrinkage of nervous tissue and lowering of the cerebrospinal fluid pressure, due to the injection of hypertonic saline. The cases which responded least satisfactorily tended to be those in which the condition was of long standing, in which possibly the emerging nerve-root gradually became attached to the chondral protrusion, as suggested by Keegan (1944). In such a case it is easy to see that shrinkage of nervous tissue would not relieve direct pressure on the root.

In 7 cases of acute rheumatic fever treated in this way the pain and swelling showed great improvement within 24 hours of dehydration. As, however, it is well recognised that such sudden changes may take place normally in the course of this disease, we do not emphasise this effect. Moreover, although the joints appeared to react favourably, the course of the disease, as shown by the ESR and the liability of further joints to become affected, was not altered. Indeed in 2 of the 3 cases dehydrated during high pyrexia the disease appeared, after 24 hours of considerable clinical and subjective improvement, to be aggravated. In 4 cases treated at a later period of the disease, however, the improvement in the joints was maintained, and no further joints became involved. It is therefore our opinion that dehydration should not be used during the pyrexial period of rheumatic fever.

Owing to insufficiency of material, due to difficulty in finding comparable cases, we had no series of controls.

EFFECT OF SUGGESTION

We have tried to estimate the possible influence of suggestion on patients subjected to this procedure. Personality was assessed in every patient and only correlated subsequently with the effect of dehydration. To our surprise those patients who had been marked as frankly unstable personalities responded in every case unfavourably. Assessment was based chiefly on general behaviour and response at the interview, evidence of anxiety reaction, tremor, insomnia, morning fatigue, frequency of micturition, tachycardia, blood-pressure, cold sweaty hands, and any history of functional disease. Further, the patient's behaviour in the ward was reported by the sister in charge.

The intelligence of every patient was also tested with Raven's progressive matrices. As is well known, those who qualify as SG 5 or below are prone to hysterical manifestations such as the prolongation and exaggeration of symptoms. Of the several patients who fell into these *categories not one did well under treatment. In wartime men of psychopathic personality tend to find an* advantage in illness, and it seems that any effect exerted by suggestion would be to the detriment of the method, which in peace-time might therefore be expected to show better results. It is not, however, intended at this stage to recommend dehydration as a therapeutic measure for routine use.

If the known neurotic personalities are removed from the group comprised of fibrositis and chronic rheumatism combined, shown in the table, the success ratio of this group increases from 3 : 1 to 4 : 1; while the results in the sciatic group remain unaltered. This unexpected result only emerged during the final analysis of the material subsequently.

ASSESSMENT OF RESULTS

The final assessment is far from easy, especially in view of the lack of a control series.

Dehydration produced no alleviation in 3 cases of severe and intractable pain due to non-rheumatic causes. The first was a case of pain persisting at the site of an old *fracture of the femur; the second was a tenosynovitis* ultimately found to be due to a splinter of wood in the tendon sheath; and the third was a particularly resistant tennis elbow. These are not included in the table.

We have tried to present our results in the most conservative way possible and have classified as failures all results showing less than 75% relief of both function and pain.

Further work along these lines might advance our knowledge and treatment of the rheumatic diseases.

SUMMARY

Evidence of the location of trigger points and fibrositic nodules in fibro-fatty tissue is summarised. An important element in the production of pain and tenderness is thought to be a non-inflammatory oedema in certain fat lobules, leading to local tension.

A method is described whereby this process can be reversed, by reducing the fluid-content of the affected tissues by inducing a clinical state of dehydration.

The clinical effect of such dehydration in cases of acute and subacute articular rheumatism, fibrositis, and sciatica is recorded and discussed.

References at foot of next page

SPASMODIC TORTICOLLIS

RESULTS OF PSYCHOTHERAPY IN 21 CASES

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AN attempt has been made in this article to assess the aetiological factors of spasmodic torticollis It has never been easy to determine how far such cases are of psychogenic origin, or how far they are more closely allied to the structural disorders with a lesion in the extrapyramidal system. In many instances the one condition dovetails into the other.

Brissaud (1895) differentiated two main classes, mental torticollis and torticollis spasm The former developed from a coordinated purposive act, the frequent repetition of which, in predisposed persons, led to its involuntary reproduction It resulted from weakness of the will, often associated with signs of mental instability, such as infantilism, impulsiveness, and obsessional neurosis Torticollis spasm, he thought, was due to irritation in the peripheral reflex arc, the spasm being uncoördinated, painful, and sometimes persisting during sleep

Gowers (1888) also differentiated the hysterical from the "true" form He believed that spasms developing under the age of 30, especially in women, were always hysterical He attributed the "true" form to an overaction of the nerve-cells in the lower brain centres Babinski (1900) maintained that most cases of torticollis spasm were due to organic brain lesions

Foerster (1928) considered it to be a localised hyperkinetic condition limited to the neck muscles and due to an organic lesion in the corpus striatum. He rejected a purely psychogenic basis on the grounds that, if it existed, the stresses and strains of the last war would have produced more cases But he postulated that in some cases the corpus striatum might be congenitally weak or diseased, causing a predisposition to torticollis which might then be precipitated by emotional stress

Wilson (1940) described cases of purely psychogenic origin, including an occupational form, similar to writer's cramp; a torticollis tic in the nature of a mannerism, and a hysterical variety corresponding to the mental torticollis of Brissaud Organic cases might follow either local infection, causing irritative lesions in the efferent nerves, or occasionally encephalitis lethargica He also thought that the constant repetition of a habit might produce irritable weakness in cell groups in the brain to which spasm might be due

Critchley (1938) differentiated 4 types psychogenic; postencephalitic, associated with an extrapyramidal motility disorder, such as chronic progressive chorea, and a progressive intractable tonic spasm of doubtful nature Patterson and Little (1943) collected 103 cases and concluded that the majority were due to a degenerative, inflammatory, or toxic lesion in the extrapyramidal or vestibular pathways, 48% showed neurological abnormalities, and 5 were definitely post-encephalitic, in only 10 did psychic factors play a significant part in aetiology.

PATHOLOGY

Since the disorder does not shorten life, there are few records of autopsies Alpers and Drayer (1937) described a case in which atrophy of the corpus striatum was demonstrated They referred to 5 other autopsies showing similar atrophy, one associated with lesions of the cerebellum, and one with extensive involvement of the right hemisphere Grinker and Walker (1933) reported a case showing chronic generalised encephalitis but without significant focal lesions Cassirer (1922) described degenerative changes in the corpus striatum in one case, with slighter changes in the optic thalami and cortex, accompanied by cirrhosis of the liver similar to that found in Wilson's disease In a case studied by Foerster (1928) symmetrical lacunar lesions were found in the lower levels of the brain ganglia and in the substantia innominata of Richert Russell (1938) described spasmodic torticollis, in a monkey, arising from a symmetrical butterfly-shaped area of softening in the subthalamic region, which histologically appeared to be an infarct.

From this scanty evidence it appears that some cases of spasmodic torticollis may be associated with lesions in the corpus striatum

TREATMENT

In the treatment of simple hysterical cases *psychotherapy* has been widely used with fair results, but the true torticollis spasm responds little if at all Clark (1912), Yaskin (1935), and Whiles (1940) report hysterical cases successfully treated by psychotherapy. Of the 10 hysterical cases so treated in Patterson's series, 6 were improved

Mechanical *immobilisation* by plaster cast or brace may produce immediate relief but it is never permanent

The importance of *infection* has been emphasised by Reynerson (1932), who reported 82 undifferentiated cases from the Mayo Clinic Foci of infection were treated and vaccines administered, as a result 19% were cured and 27% improved

Sedatives have little effect On the assumption that some of the cases are postencephalitic, stramonium, atropine, hyoscine, and amphetamine are often tried with some successes (Myerson 1942)

During the past 20 years *surgery* has been increasingly used for the relief of spasm, and with the modern technique devised by Finney (1925) and modified by Dandy (1930) and Foerster (1933) the results are encouraging Finney (1925) reports improvement in 28 out of 32 cases, Olivecrona (1938) stated that in a series of 33 patients 60% were relieved and able to work Out of 44 cases treated surgically in Patterson's series 15 were much improved and 11 slightly improved.

REVIEW OF CASES

During the past 10 years, out of 2500 consecutive admissions to Jordanburn Hospital for all forms of psychoneurosis there were 21 cases of spasmodic torticollis All were referred because of a supposed psychogenic basis, and cases with obvious neurological signs were excluded The main features of the cases are summarised in the accompanying table

The average age was 33, 10 were males and 11 females In 11 the head was turned to the right, in 8 to the left, and in 2 to both sides Pain was severe in 7 but did not bear any relationship to the severity or frequency of the spasm; all complained of stiffness and discomfort. The spasm was more severe when the patient was nervous or excited, and, except in case 21, disappeared during sleep

None of the patients had had any serious illness. Except in case 20, none had previously suffered from tics or habit spasms, and there was no history of similar disorders in their families

Eleven had records of being poor scholars, and of frequent changes of employment, and were considered to be below average intelligence, 2 tested on the Terman-Merrill scale had mental ages of 11 and 12

In 16 there was a shy anxious immature disposition From childhood they had been nervous and timid, often overdependent on their families, unable to mix socially or to take responsibilities They lacked self-confidence and initiative This corresponds to the state of infantilism which Brissaud associated with mental torticollis. In 3 of this group the immature personality was associated with an anxiety neurosis; 2 others, besides their immaturity, showed hysterical personality traits, *belle indifférence*, self-indulgence, and a tendency to ignore or forget adverse criticism Of the remaining 5 cases in this series, one was a psychopathic personality with a history of juvenile stealing, alcoholism, and gambling, and 4 were well-adjusted.

Details of the onset of the first spasm were carefully

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SUMMARY OF THE MAIN FEATURES OF 21 CASES OF SPASMODIC TORTICOLLIS

Case no.	Sex	Age	School and work record	Spasm	Pain	Side	Precipitating factor	Personality	Remarks	Result on Discharge	Final result
1	F	20 s	Bad	Slight	Slight	R	Fear of work	Immature shy		No change	
2	M	33 m	Good	Severe		R	Army training	Overconscientious		Much imp	Much imp
3	F	18 s	Bad	Slight		L	Work	Immature spoilt		"	"
4	F	20 s	"			L	Slight trauma	Immature anxious		Recovered	Recovered
5	F	23 s	Average	Moderate		R	Worry at work	Immature lazy	Hysterical		"
6	F	45 m	"	Severe	Severe	R	Marriage	Inadequate spoilt		Sl imp	Sl imp
7	M	44 s	Bad	Moderate	Slight	L	Overwork	Immature lazy	Hysterical	"	
8	F	30 s	Average	"		R	Worry at work	Immature, timid selfish		Recovered	Recovered
9	M	30 m	"	"		L	Bereavement	Anxious, timid immature	Anxiety neurosis		"
10	F	40 s		"	"	L	"	Immature anxious dependent		Much imp	Much imp
11	F	50 m	Bad		Severe	R	Trauma overwork	Inadequate sensitive		Sl imp	Worse
12	M	34 m	Average	"		Both	Bereavement	Inadequate anxious		No change	
13	M	38 s		"	Slight	R	Engagement	Immature anxious	Anxiety neurosis	Much imp	Much imp
14	M	29 s	Bad	Severe	Severe	R	Narrow escape from accident	"		No change	No change
15	M	22 s	Average	Moderate	Slight	L	Illness in family		Anxiety neurosis	Recovered	Recovered
16	M	56 s		Severe	Severe	R	Exposure to cold	Well-adjusted	Osteo-arthritis	Much imp.	Much imp.
17	M	34 s	Bad	"	Slight	R	Army training	Inadequate	Tuberculous spine	No change	No change
18	M	20 m	"	Slight	"	L	None	Psychopathic delinquent		Sl. imp	Worse
19	F	28 m	Average	Severe	Severe	R		Well-adjusted	Neurological signs present		Sl imp
20	F	18 s	Bad	Slight	Slight	L	"	Nervous timid sensitive	Previous chorea	"	
21	F	48 m		Severe	Severe	Both	Menopause	Well-adjusted			Sl imp

Sl imp = Slightly improved.

elicited. In most cases it was gradual and attributed by the patients to cold, trauma, overwork, &c. In 5 the spasm could be traced to a voluntary purposive act which in certain emotional settings became involuntarily repeated. A telephonist had during the course of her work to turn her head to the side. During a period of overwork and anxiety this movement was repeated involuntarily, producing a moderate degree of spasmodic torticollis.

Two men developed the disorder during army training which involved turning the head sharply to the side. Case 16, following exposure to cold and draughts in a building damaged by bombs, developed a severe osteo-arthritis of the spine. To minimise the pain he held his head stiffly. Gradually a severe involuntary retrocollic spasm developed with clonic spasms jerking the head to the right. Both this man and case 17, who had a tuberculous spine, illustrate the way in which torticollis may be associated with local infection or injury.

In 2 patients the disorder started suddenly and dramatically. Case 15 woke to hear his mother telling him that his sister's finger had been amputated. He was startled and felt his head jerk. This jerk persisted and developed into typical spasmodic torticollis. Case 14, hearing a shout from his companions looked up, turning his head sideways, and saw a load about to fall on him. He was able to jump clear but could not forget that terrifying moment. An intractable and increasingly severe spasmodic torticollis developed, as a result of which he was never able to work again.

4. ILLUSTRATIVE CASE RECORDS

CASE 2.—Male, 33, married, insurance agent. Self-conscious and shy but conscientious and ambitious. He had held a responsible post for 12 years. When conscripted he settled down fairly well to army life and performed clerical duties for 3 years. When his unit went abroad he was transferred to another, but felt that he could not face starting over again. During infantry training which involved forcible movements of the head and which he particularly disliked, spasm started suddenly in the left sternomastoid and gradually spread to other neck muscles. After 3 months in hospital he was discharged from the army. He was unable to work, and his previous employers threatened to discharge him if he was not better in a month.

When he reported at Jordanburn Hospital in August 1944 he was anxious and depressed. There was severe tonic spasm of the neck muscles, pulling the head to the right, and clonic spasm whenever he tried to move the head. Curiously enough the head could be moved passively in all directions; and, if it was supported with a finger, the spasm disappeared. After 6 weeks' treatment with psychotherapy and suggestion under light Sodium Amytal narcosis the spasm had almost disappeared, and he was able to return to work.

There seems little doubt that the sudden onset of torticollis at a time of stress was a hysterical reaction. The patient was "turning away" from his difficulties. The torticollis achieved its object and he was discharged from the army, but instead of disappearing the spasm persisted as a tiresome habit. It here appears to be an involuntary repetition of a routine purposive act performed during physical training. The way in which relaxation of the spasm could be produced by supporting the head with the finger is an illustration of the *geste antagonistique*. The older neurologists often observed this phenomenon and thought it indicated a hysterical origin. Patterson, Wilson and others believe that the gesture may produce afferent proprioceptive impulses which influence the torticollis through a definite neurophysiological mechanism.

CASE 6.—Female, 45, married, no children. A delicate spoilt anxious woman, shy, self-centred and over-dependent on her family. She had "enjoyed" ill health all her life and had been unable to work for longer than 18 months. At the age of 35 her right leg became weak and for 6 months she could not walk. This was diagnosed as hysteria, and she recovered gradually. At the age of 42 she married a widower

20 years older than herself, largely because she wanted security and a home She found the responsibilities of married life greater than she expected Great difficulty was experienced in their sexual relationship, she was afraid of pregnancy and found coitus painful and distasteful She decided that her marriage had been a mistake Within a few days she noticed weakness in her neck, so that the head fell to the right Severe tonic spasm gradually developed, so that her right ear touched her shoulder. Attempts to straighten the head resulted in painful clonic spasms

She was treated at 3 different hospitals with electricity, massage, rest, immobilisation, and manipulation with no avail When admitted to Jordanburn Hospital in July, 1942, she had been in bed for 8 months Psychotherapy was supplemented with a course of electric convulsion therapy. Her physical condition and mental attitude improved greatly, she returned home and undertook all household duties The tonic spasm, however, persisted, and was still present when she was seen 2 years later

This case illustrates the hysterical reaction to difficulties. The patient became ill, avoided her responsibilities, and so escaped her marital obligations

CASE 9—Male, 30, married, leather sorter A shy timid anxious personality lacking in drive and ambition After leaving school he was apprenticed to a leather sorter and remained in the work, in which he was not interested and had no chance of promotion He was overdependent on his family and made few friends outside He married a friend of his sister after she had been coming to the house for 5 years. After the sudden death of his sister he became anxious and shaky and began to notice twitching of the neck. He had fainting attacks, pains in the chest and side, headaches, numbness of the fingers, and breathlessness Spasm of the right sternomastoid became more severe and spread to other neck muscles, jerking the head to the left The symptoms were aggravated when his father died a few months later. He responded well to suggestion and reassurance under light hypnosis and was discharged recovered after 6 weeks He subsequently joined the army, graded B owing to varicose veins, and, apart from occasional twitching in the neck when excited, remained free from symptoms

This man illustrates the anxious inadequate personality common to many of the patients. He reacted to emotional stress with physical symptoms, of which torticollis was only one

METHOD OF PSYCHOTHERAPY

Psychotherapy was used in all cases in an attempt to correct the faulty emotional reactions and attitudes of the patient—i e, his neurosis—and in so doing to alleviate or banish the torticollis The emotional and environmental influences which had moulded their previous personalities were ascertained as far as possible. A detailed analysis was made of the setting in which the torticollis first developed The patient's dominant drives and interests and emotional reactions and attitudes at that time were investigated In intelligent and coöperative patients good results were achieved by giving them insight or an explanation of the way in which the torticollis had arisen. Where the patients were of poor intelligence recourse had to be made to suggestion, which also plays a part in insight or explanation The influence of suggestion was much enhanced by inducing a mild hypnotic or narcohypnotic state

RESULTS

Five patients were completely free from spasm when discharged, and although they all had slight recurrences when nervous or excited these did not persist In all these the disorder was considered to be of psychogenic origin Five others were much improved and able to return to work Seven were slightly improved, and although the torticollis was still troublesome they were able to return to their usual occupation. In 4 there was no change.

Many of these patients were of poor intelligence and had difficulty in following psychiatric explanation Two left without completing treatment Two hysterical patients were uncoöperative, they found the symptom useful and did not really want to be cured

Seventeen were followed up; 4 could not be traced. In 13 the improvement was maintained and often continued after the completion of treatment. Two, who had benefited slightly in hospital, gradually deteriorated, and four years later their condition was worse than when admitted.

DISCUSSION

Most writers differentiate functional from organic torticollis, but the exact criteria have never been defined. Where the personality is immature and neurotic, hysteria is usually diagnosed Yet, if an immature personality were of such ætiological significance, we should expect spasmodic torticollis to be much commoner than it is. There must therefore be additional causal factors. Moreover, it is not impossible for a neurotic personality to have organic cerebral lesions. Indeed, neurotic traits are often aggravated by, and in some cases may arise from, such lesions—e.g, encephalitis lethargica

Of these 21 patients, 16 were inadequate neurotic personalities, but, although it may be probable, we are not justified in regarding the torticollis as psychogenic on this evidence alone In a few it appeared to be a true conversion hysteria, in others part of an anxiety state often associated with tremor in other parts of the body. It is interesting to speculate about why this rare symptom should arise and what additional causal factors were present. Brissaud's theory, that a coördinated purposive act may in certain emotional settings become involuntarily repeated, certainly offers an explanation in some of the cases I have mentioned In them torticollis appeared to originate from movements made during work or physical training A second way in which the spasm originated was after an emotional shock causing the head to be jerked suddenly sideways. Thirdly, local disease or injury may possibly cause a focus of diminished resistance, irritation, or local spasm, which, in its turn, may provide a starting-point for the disorder. Wilson considered the last to be the commonest cause.

Three patients in this series had no neurotic traits and were well-adjusted personalities One had neurological signs consistent with an extrapyramidal lesion, one had osteo-arthritis of the spine, and the third, apart from poor intelligence, had no signs or symptoms that could suggest a basis for the disorder. It is possible that these were all organic cases having some toxic or degenerative changes in the extrapyramidal system, but without post-mortem evidence such a diagnosis must be tentative If spasmodic torticollis is one of the results of such a lesion, it is difficult to explain why it should be so rare.

Foerster considered that in some people the corpus striatum might be congenitally weak or diseased in such a way that they would be predisposed to torticollis In such persons the disorder might be precipitated by emotional stress in the psychogenic group or by a chronic degenerative process in the organic cases. This is a most attractive hypothesis, which helps to explain the cause of the disorder, but there is as yet no pathological evidence to support it

As regards the treatment of spasmodic torticollis, there are some who consider that, since psychotherapy requires so much time and patience and since a cure cannot be guaranteed, surgery should replace it. In this series, although only 5 were cured, 10 were much improved This compares not unfavourably with surgical results Whereas surgical treatment merely relieves the symptom, psychotherapy attempts also to cure or modify the underlying neurosis It is therefore of great value to the patient, particularly where the personality is of the anxious, immature type, when a fuller understanding of his difficulties will help the patient to adapt himself to his environment Even where the spasm was only slightly improved, the patients' attitude towards their illness and their surroundings was so much better that most of them were able to return to their usual occupations In this respect even the cases in which an organic lesion was suspected showed some improvement It may be concluded therefore that psychotherapy is of undoubted value to the patient in this condition and unless signs of gross organic disease are present should always be tried.

SUMMARY

The literature is briefly reviewed on the ætiology, classification, pathology, and treatment of spasmodic torticollis

A survey is given of 21 cases treated at Jordanburn

Hospital, of which 18 were considered to be of psychogenic and 3 of possibly organic origin

Treatment by psychotherapy led to 5 being cured, 5 much improved, 7 slightly improved, and 4 unchanged on discharge from hospital

It is concluded that, except in cases showing gross signs of organic disease, psychotherapy is the treatment of choice

I wish to thank Prof D K Henderson, who suggested this problem, for his encouragement and advice, and the members of the medical staff past and present, for the use I have made of their case records.

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'CELLOPHANE' DRESSING FOR SECOND-DEGREE BURNS

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THE major advances made during the war in the treatment of burns have been based on well-defined principles:

(1) Secondary infection (or hospital infection, as it is better termed) must be avoided
(2) The burn area is initially sterile, and infection comes later Hence strict asepsis is essential in dressing burns; gowns and masks are worn and instruments are sterilised by boiling
(3) Loss of fluid may require administration of plasma

From these principles has emerged the 'leave-it-alone" technique Men arriving in a state of severe shock due to pain, loss of plasma, absorption of toxins, several changes of dressings, or long journeys in ambulances will always do better in a clean bed under the influence of morphine than when rushed into an operating theatre In such cases the dressing should be postponed till next day, and done under a further dose of morphine

Superficial cleaning has of late been recommended, and this toilet, however extensive, should be painless Blisters are cut away entirely, until viable adherent skin is reached Coagulated serum is carefully removed All dead and non-adherent skin is peeled off and cut away Epidermis which is apparently little damaged, but which peels easily, must be completely removed because if left it may be a nidus of infection The areas are then washed with sterile saline under the pressure of a Higginson syringe The saline will lift up small areas of devitalised skin, previously overlooked, and these must be removed

A sulphonamide powder may now be applied to the burn; but in dressing cases already treated in this way it may be inadvisable to repeat the local application since excessive quantities of the drug may be absorbed locally In my opinion there is no indication for sulphonamides by mouth, because there is no generalised sepsis.

I do not consider it advisable to apply other preparatory antiseptics Usually the whole area has already been covered with one or more of the antiseptic creams, ointments jellies, or paints. Unbroken blisters are very often found to be full of purulent fluid, and a sheet of frank pus may cover the denuded areas within 24 hours of the injury

CELLOPHANE DRESSING

The object of this paper is to suggest that, after cleaning, the burn should be covered with 'Cellophane' instead of the more commonly used tulle-gras I first used cellophane for this purpose when a prisoner-of-war in Italy, where routine daily dressing of extensive second-degree burns was killing many of our men It was applied as a protection primarily against Italian conceptions of treatment, but the results were so gratifying that I became convinced of its value I have since treated 55 cases in the BLA in this way

The cellophane was obtained from a transfusion unit and was sterilised in steam under 10 lb pressure for 20 min. Applied to the burn, it forms a semipermeable membrane covering—*not* an occlusive dressing

After sulphonamide powder, penicillin powder, 'Marfanil,' or 'V 187' has been insufflated over the carefully cleaned burn area, a single sheet of cellophane is laid over it and fixed at the edges with strips of adhesive cellophane or tape Burnt hands are completely covered with a single sheet passing round the fingertips: it is slit between the fingers and gently moulded round the separated digits. A burnt face is enclosed in a loosely fitting bag fashioned from two sheets, with slits for the mouth and nostrils. Ears, if burnt, must be separated from the skull with a separate square of cellophane

The damaged area is next covered with a single sheet or layer of gauze Digits are wrapped individually A cotton wool layer 1 in thick follows, and the whole limb (for example) is bandaged moderately tightly, special care being taken of the digits, which are bandaged individually This moulds the cellophane firmly on to the contours of the limbs and fingers

When the condition of the patient permits, the bandages, cotton wool, and gauze are then removed and the damaged areas are left exposed under the cellophane In the more severe cases the areas will begin to steam immediately, showing that water is transuding through the dressing This transudation continues for some hours, leaving a clean dry painless mobile healing area under the transparent covering which is bandaged up only at night for protection When healing is complete, the cellophane is easily stripped off

The cellophane, besides preventing infection with secondary organisms, prevents the protein-content of the plasma from escaping; hence, from the moment of its application, loss of protein ceases. Inflammatory processes readily subside under its smooth and innocuous surface, and regeneration of skin takes place quickly Finally, by preventing the escape of proteins, it avoids the rigid compressing effect of serum clot, which with other dressings tends to form a rigid splint as it seeps into the layers of gauze Limbs and digits can move freely and painlessly from the first, since the cellophane is flexible and allows a certain amount of sliding movement when the burn is in the tacky stage After a day or so the cellophane cracks at the flexures but it remains adherent over all the other areas.

RESULTS

In 55 cases the average time between the application of the cellophane and complete healing was 9 days *Infection before treatment was no contra indication to* the application of cellophane, for burns healed normally under a thin layer of inspissated purulent serum

Patients stated that pain disappeared as soon as the cellophane was applied

SUMMARY

After a single thorough cleaning of the area of a burn, and after sulphanilamide or other powder has been insufflated, a dressing of cellophane is applied directly to the surface of the burn and then covered with a single layer of gauze and a layer of cotton wool an inch thick.

Later the gauze and cotton wool are removed leaving only the cellophane

By this means full painless movements are possible from the first, further loss of plasma is prevented, and risk of secondary infection is obviated

Pain disappears on application of the cellophane and healing which can be observed through the cellophane, is rapid Repetition of painful dressings is avoided

I am grateful to Brigadier Ian Fraser D.S.O. for the privilege of treating some of these men and for his interest continued encouragement, and active collaboration in this work

ANAEROBIC STREPTOCOCCAL MYOSITIS

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STREPTOCOCCAL infection of muscle simulating gas-gangrene due to clostridia in war wounds has been described by MacLennan (1943a and b, 1944), who says that its recognition is important since it calls for most conservative surgical treatment We therefore report the following case, which, occurring in civil practice, could be studied in greater detail than MacLennan's cases It was thought to be a clostridial myositis until the bacteriological report was available

CASE-RECORD

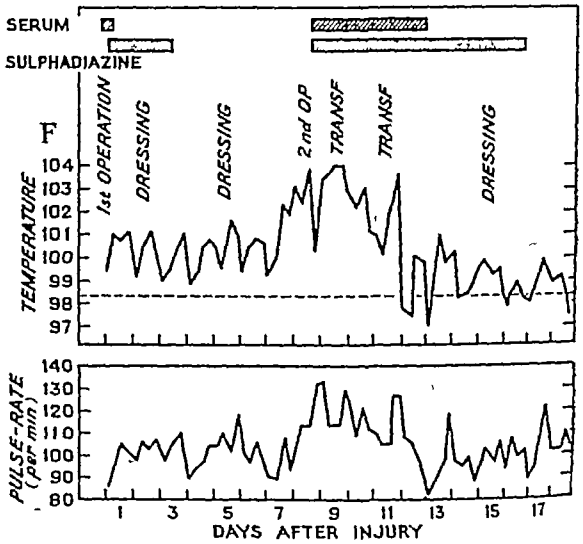
A man, aged 23, was admitted to hospital on April 4, 1944, a few minutes after sustaining an injury to the left leg in a street accident His leg was caught by the front wheel of a bus, which dragged him along a few feet but did not pass over the leg. On admission he was a little shocked and obviously had a severe injury to the soft tissues of the leg Pulsation could be felt at the ankle in the posterior tibial artery but not in the dorsalis pedis There was no loss of sensation in the foot, the toes and ankle could be actively dorsiflexed A radiogram showed a fracture of the neck of the fibula and the tibia intact At operation 1¾ hours after admission the skin of the back of the calf on the medial side was found to be vertically split and stripped off the deep fascia almost round the limb The deep fascia was much torn, and the gastrocnemius, soleus, peroneus longus, and anterior tibial muscles were damaged The injury extended up to the medial side of the knee, where the quadriceps aponeurosis was torn without opening the joint The lateral popliteal nerve and its musculocutaneous branch were intact

The skin was incised at each end of the split to improve access to the deep parts Obvious dirt was removed, the deep fascia was widely incised, and the more severely damaged fascia and muscle were excised Counter-incisions for drainage were made in the popliteal fossa and on the lateral side of the calf The wounds were dressed with soft-paraffin gauze, and a plaster cast was applied. Antitetanic serum and polyvalent clostridial antitoxin were given, and sulphadiazine by mouth was started after operation On the 2nd day, when the leg was dressed, the wounds were found to be clean, and part of the long wound was sutured, although there was some doubt about the viability of the medial flap There was no effusion in the knee The plaster was reapplied Sulphadiazine was discontinued on the 3rd day, although there was fever since the injury The leg at this time was not very painful The dressing was repeated on the 5th day owing to the persistence of fever, but the wounds did not appear to be seriously infected On the 7th and 8th days there was a further rise of temperature and pulse-rate; the patient felt ill and complained of increasing pain in the leg Circulation and sensation in the foot were not impaired

On the 8th day the leg was examined again under anæsthesia The whole calf was greatly swollen, and the skin on the medial side of the loosely sutured long wound was obviously dead over a width of 4 cm and a length of 20 cm All stitches were removed, and the dead skin was excised. The long medial wound was explored, the surface of the exposed gastrocnemius was necrotic, but the deep part of the muscle when incised looked healthy and twitched freely The necrotic fascia on the surface was excised, and the gastrocnemius was split to expose the medial part of the soleus, which appeared to be healthy, although vessels passing through it were found thrombosed The counter-drainage incision on the lateral side was then explored, and a large amount of thin bloody pus and gas escaped Through this wound the outer part of the soleus was found to be swollen, firm, and inert On section it was paler than normal and opaque, looking like cooked meat The wound was extended to the length of the calf, and the whole of the outer two thirds of the soleus was excised The deeper muscles and the inner third of the soleus appeared healthy The wounds were dressed with soft-paraffin gauze and the limb splinted with plaster.

On the appearance of the wound a diagnosis of clostridial myositis was made, and 4 hourly administration of polyvalent antitoxin and a course of sulphadiazine were started Antitoxin was given 4-hourly for 2 days and then 6 hourly for 5 days, being discontinued when it was reported that the infection was streptococcal. Sulphadiazine was continued for 8 days, the level in the blood being estimated once on the 5th day at 7 9 mg per 100 c cm On the 2nd and 4th days of this course blood was transfused. On the 4th day after the last operation, the 12th since the injury, there was a great improvement in the general condition, and the temperature which had been swinging to 104° F, began to fall On the 15th day after injury the leg was dressed again, and the wounds looked healthy, but the leg was much swollen, and the two long incisions were gaping widely. Sulphathiazole proflavine powder was dusted on the raw surfaces, which were then covered with soft-paraffin gauze and enclosed in plaster The limb was elevated to reduce the swelling On the 22nd day the leg was dressed again as before and the lateral wound was sutured. Although the swelling had subsided, it was impossible to suture the medial wound owing to the skin loss On the 31st day dressing was done again and the stitches were removed from the lateral wound, which had healed. After this, daily dressings were done to prepare the leg for grafting

On the 37th day a large dermatome graft was cut up into pieces about the size of postage stamps, which were applied to the large raw area About 75% of the grafts took, and the small spaces between were rapidly bridged by new epithelium The leg was healed 10 weeks after the injury At one time there was a tendency to flexion contracture at the knee, but this rapidly disappeared when the raw area was grafted Although there was no injury to the lateral popliteal nerve,



there was a definite weakness of dorsiflexion of the ankle and toes at the time of grafting, which is recovering slowly There was no sensory loss, and the weakness was probably the result of disuse It was difficult for the patient to exercise his dorsiflexors owing to the extensive injury to the calf

BACTERIOLOGICAL REPORT

The results of the bacteriological examination of the wound are given in the table. The aerobic organisms and anaerobic bacilli were in every way typical of their species The anaerobic cocci resembled those of Prévot's (1925) group A—I e, they were strictly anaerobic even after prolonged subculture They occurred in pairs, irregular clusters, or short and often irregular chains; they failed to produce hæmolysin, attack coagulated serum, liquefy gelatin, or to form indole They could be differentiated into a non-saccharolytic type that did not form gas in nutrient-agar shake culture and in cooked-meat medium; and a saccharolytic type that formed gas in both media, although the foul odour commonly attributed to the anaerobic streptococci was slight or absent These types have been arbitrarily labelled I and II In the saccharolytic type positive sugar reactions were difficult to elicit, but acid and gas were produced in glucose, maltose, mannitol, and sucrose, but not in salicin or lactose. It is noteworthy that although the presence of gas was an outstanding feature of the lesion, no foul odour was noticeable

* In receipt of a grant from the Medical Research Council.

SUMMARY OF BACTERIOLOGICAL FINDINGS (FIRST OPERATION ON DAY 0)

Days after wound long	Surgical treatment	Site of specimen	Direct smear	Cultural findings: Str pyogenes	Anaerobic cocci I	Anaerobic cocci II	Staph aureus	Others
2–5	Dressings							
8	Operation	Muscle	+ Gram pos. cocci long chains	++++	±	±	±	+++ Non haemolytic strep ++ *Bacillus sp* + *Cl. welchii* ± *Micrococcus sp*
		Lateral side of calf	+++ Gram pos. cocci long chains +++ Gram pos cocci clusters + Pus-cells	++++	±	±	++	++ *Cl. welchii* ± *Strep haemolyticus* Lancefield C ± *Strep. viridans* type
		Upper part of wound posteriorly	+++ Gram pos cocci short chains & small groups			+++		++ *Cl sporogenes* ++ Non haemolytic strep
		Lower part of wound posteriorly	No organisms seen	±		++		++ *Cl sporogenes* + *Strep haemolyticus* * + Non haemolytic strep
15	Dressing		+ Gram pos cocci long chains ± Gram pos bacilli 1 × 4μ + Pus-cells	++++	±		+++	++++ *Cl welchii* ++ Mucoid coliform bacillus ± Diphtheroid
22	Dressing: lateral wound sutured	Lateral side of calf	+++ Gram-pos cocci long chains +++ Pus-cells	++++	±	±	++	+++ *Ps pyocyanea* +++ *Bacillus sp* ++ *Bact alcaligenes* ++ Diphtheroid
		Middle of calf	+++ Gram pos. cocci chains +++ Pus-cells	+++	±	±	+	+ Diphtheroid
31	Dressing		± Gram.-pos cocci pairs ++ Pus-cells	++++	±	±	+	+ Diphtheroid
32–33	Dressings							
34	Dressing	Back of calf proximal end	+++ Gram pos cocci chains +++ Pus-cells	++++		±	+	
		Skin proximal end	Not examined	±		±	±	
		Skin distal end		±	±			± Diphtheroid
35–36 37	Dressings Graft from rt. leg							
42	Dressing	Sinus	Not examined	+++				+ *Micrococcus sp* ± *Vibrio alkaligenes*
		Graft		++++		+	++++	

* Not belonging to either of Lancefield's groups A, B, C, and O

Under "Direct smear" +++, ++, + and ± indicate relative numbers of morphological types seen. Under "Cultural findings" ++++, +++, ++, + and ± indicate relative numbers of colonies appearing in direct plate cultures and ± indicates growth from cooked meat medium only after either 2 or 7 days incubation.

Examination of the specimens taken at operation on the 8th day showed the bacterial flora of the excised muscle to be very similar to that of the thin bloody pus from the counter-drainage incision. The bacteria of the upper and lower margins of the original wound were also alike but differed from the flora of the muscle and exudate. In general, the bacteria recurring in later specimens—i.e., *Strep. pyogenes* (Lancefield's group A), anaerobic cocci (types I and II, *Staph aureus* (coagulase-positive), and *Cl welchii*—were those originally found in the muscle, and may be presumed to have been the chief infecting agents.

The finding of only gram positive cocci in stained direct smears taken on the 8th day suggests that they dominated the infection, no bacilli were seen though on a medium optimum for its detection, a scanty growth of *Cl. welchii* was obtained by culture. On the 15th day, when bacilli appeared in the direct smear and *Cl welchii* grew profusely in culture, the patient was already recovering. *Cl. welchii* may therefore be considered unimportant as the cause of the progressive gangrene and toxaemia. This view is supported by the occurrence of numbers of healthy pus-cells in direct smears. In infections with *Cl welchii* pus-cells are usually scanty and degenerate.

The predominance of *Strep pyogenes* in the plate cultures suggests that it was a chief infecting agent. However, gas was evident in the wound exudate, and it is therefore probable that the only gas-forming organism in the muscle apart from *Cl welchii*—i.e., the type II anaerobic coccus—was also important in the infection. The scanty growth of the anaerobic coccus may not necessarily indicate a scanty infection in the wound but be due to a selective action by the culture media, whose growth promoting properties are more favourable to *Strep pyogenes* than to anaerobic cocci.

The muscle infection, apparently due to the combined action of *Strep pyogenes*, the type II anaerobic coccus, and possibly of *Staph aureus* is similar to the streptococcal myositis described by MacLennan. Streptococcal myositis is a gas gangrene due to anaerobic streptococci in association with various aerobic pyogenic cocci. *Strep pyogenes*, *Staph. aureus*, or *Strep viridans*. Anaerobic spore bearing bacilli were not present in any of MacLennan's cases of streptococcal myositis. In this case the findings suggest that *Cl. welchii* had little aetiological significance, and the concomitant presence of healthy pus-cells bears out MacLennan's contention that when clostridia and cocci are present together, predominance of cocci and presence of pus-cells exclude clostridial myositis. The importance of direct microscopical examination in indicating the predominant infection cannot be too strongly emphasised.

Tested by the method of Harper and Cowan (1945), all the anaerobic cocci proved insensitive to sulphanil

treating several types of urinary tuberculosis with prolonged sanatorium care and streptomycin Six months should be regarded as the minimum of sanatorium care while longer periods of time are often necessary and ninety to 120 days of streptomycin therapy are recommended The dosage most often effective has been 1 5 to 2 gm per day The types of genitourinary tuberculosis that are now treated in this fashion include bilateral renal tuberculosis, tuberculous cystitis following nephrectomy, unilateral lesions of the kidney where there are no pyelographic evidences of the disease, also cases of genital tuberculosis

Nephrectomy may not be the logical procedure in clinically proven unilateral renal tuberculosis It may be wiser to place such a patient on streptomycin, rest and sanatorial care for a period of sixty days It has been reported that even ulcerative renal lesions will sometimes heal during treatment with streptomycin When studies indicate conspicuous evidences of healing the regimen should be continued for another period of sixty days If, however, there is no improvement after sixty days of initial treatment and tubercle bacilli and pus remain in the urine—nephrectomy would be indicated Postoperative streptomycin therapy should be continued for sixty days longer and the patient kept at rest for the prescribed six month period or longer if necessary. There is no question that the future of the patient nephrectomized for renal tuberculosis has been made more attractive, since surgery alone only gave the patient an even chance for survival Traumatic spread of the disease is prevented, healing of the incision is more prompt, and the likelihood of miliary dissemination during and after operation is diminished

Chloromycetin.—Chloromycetin has been a more recent addition to the family of antibiotics It has been recommended in treatment of urinary infections caused by gram-negative organisms Experience with this drug is limited In intractable cases of cystitis patients have reported benefits. It is interesting to note that many patients who have a persistent urinary tract infection despite attempts to clear up the etiologic factor, will report some improvement when the newer chemotherapeutic agents and antibiotics are employed It appears that they lose their effectiveness just as promptly as their predecessors after a period of trial At present the effectiveness of chloromycetin cannot be evaluated

Mandelic Acid and Its Derivatives.—These enjoy a wide use in the treatment of bacillary infections of the urinary tract Mandelamine is the most popular of urinary antiseptics in this group

It is particularly free of toxicity and efficacious in those cases which are sensitive to the sulfonamides In postoperative transurethral procedures mandelamine is widely used The dosage of 1 gm of mandelamine three or four times a day for seven or ten days is adequate to produce and maintain antibacterial concentrations in the urine In acute infections of the urinary tract caused by gram-negative organisms the use of mandelamine is contraindicated because it is apt to produce renal irritation It should be used for patients who cannot be hospitalized and where streptomycin cannot be employed in logical sequence I find it very useful in routine office procedure where the urine is infected with B coli, in women with chronic cystitis

Pyridium.—Pyridium must be included in a discussion of urinary antiseptics It enjoys a wide popularity It is probably the most common urinary antiseptic because it is relatively nontoxic and the physician does not need to be concerned with the side effects of the sulfonamides, or the relative sensitivity of the antibiotics Pyridium has a soothing effect on the mucosa of the urinary tract and the acute symptoms of burning on urination, frequency of urination, and dysuria are diminished Psychologically the patients possibly derive some benefit from its use because of the beautifully tinted orange color of the urine Two or three tablets of pyridium three times a day usually are sufficient to produce a therapeutic effect It apparently is common procedure, in office practice, to give a single injection of penicillin of 300,000 units and maintain oral medication with pyridium until the next visit of the patient This may be good therapeusis if the infection of the urine is chiefly due to a coccus, otherwise the penicillin is wasted The rapidity of therapeutic response in any urinary infection depends upon a proper urine study

Arsenicals.—A group of a bacterial or sterile pyurias presents a difficult problem of management Penicillin and streptomycin are of no value The sulfonamides produce no marked change in the urine It is important to rule out tuberculosis The relationship of abacterial pyuria to Reiter's syndrome—a nonspecific urethritis, conjunctivitis and arthritis—remains unsettled The smears and cultures fail to show any organisms by all known laboratory technics During the late war we were told that many soldiers developed a nonspecific urethritis and prostatitis The causes were numerous, prolonged train and truck rides, fatigue, physical and mental strain, and unsatiated sexual unpulses causing a congestive prostatitis The arsenicals are the only known specific remedy

Neoarsphenamine given intravenously in a dosage of 0 3 or 0 45 gm in one, two or three doses at intervals of five or seven days is the only requirement The results are dramatic Since rest and sedation alone will sometimes relieve the acute symptoms, the response to arsenotherapy is considered specific only when all other treatment has failed, when arsenicals produce an immediate effect and when complete eradication of all signs and symptoms is the end result

The value of the arsenicals in staphylococcic pyurias is a well known clinical fact Where resistant strains of staphylococci develop as a result of penicillin therapy the arsenicals may be very useful While aureomycin may develop into a satisfactory adjunct in staphylococcic-penicillin resistant cases, mapharsen in dosage of 0 06 gm for five to seven injections at intervals of four days is preferred by some clinicians because of its low toxocity

SUMMARY

It is well to study each case of infection of the urinary tract carefully and try to ascertain all the clinical data essential to the successful termination and eradication of the infection

The fundamental principle to bear in mind is that an adequate and free urinary passageway is the single and most important requirement

The careful study of the urine in order to determine the infective organisms is necessary in order to employ the specific remedy to eliminate the infection

Intelligent management of infection of the genitourinary organs requires just a little more persistence on the part of the physician if the patient is to enjoy the recent advances of chemotherapy and antibiotics

CUMULATIVE INDEX

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SYMPOSIUM ON ACUTE MEDICAL EMERGENCIES

From the Benjamin Franklin Clinic of the Pennsylvania Hospital

FOREWORD

Teamwork is the essence of the practice of medicine at its best Research has progressed recently as never before and it has done so in direct proportion to the growth of suitably selected and integrated groups of investigators Similarly, the increasing complexities of medical practice are such that certain types of problem cases are being solved only by compounding of the investigational efforts of specialists in different branches of medicine Diagnostic problems concerning the gastrointestinal tract are good examples, the solution of which lies in the wise evaluation of the overlapping opinions of surgeon, psychiatrist, gastroenterologist and internist Intractable headache may be the object of study by the neurologist, neurosurgeon, allergist, psychiatrist and internist before the proper perspective for a clearcut diagnosis is achieved Such examples of teamwork and its advantages in the diagnosis of disease in problem cases are legion The same is true in therapy in which the joint efforts of specialists in the management of the patients with bleeding peptic ulcers, diabetic coma, visceroptosis with renal colic, unexplained bleeding, and jaundice lead to better care through coordinated use of recent advances in all fields

The complexities surrounding the diagnosis of and therapy for these and other problem cases and the successful outcome of teamwork has been one of the biggest factors in the development of group or diagnostic clinics How such clinics may serve the profession as a whole in the best possible manner may be controversial However, basing conclusions on approximately 2000 patients studied in the Benjamin Frank-

lin Clinic of the Pennsylvania Hospital there is much evidence that such a clinic situated in a densely populated center serves best by limiting its scope strictly to the teamwork solution of referred diagnostic and therapeutic problem cases

This symposium dealing with acute medical emergencies is presented with the purpose of extracting from the enormous literature what had proved good and practicable in our hands Advances in the management of *phlebothrombosis* and related difficulties have a wide range of application Exposure of the *headache* problem to the elimination table formula and simplification of therapy, in a similar manner, has proved merit In bringing the therapy for *diabetic coma* up to date, measures are presented which have kept the mortality from this complication of diabetes at zero for over two and one-half years Practical guides in the management of *bleeding in general*, and from the *gastrointestinal tract* in particular, and of *status asthmaticus* are included The clinical diagnoses of *emergency conditions of the chest* and recommended therapies are simplified and certain warnings are sounded *Cardiac emergencies* are among the most common of the immediate demands made upon a physician The outcome may depend upon the promptness with which the diagnosis is made and the speed with which appropriate treatment is begun These matters are dealt with in a manner which will appeal to the general practitioner who has to face these problems daily The correction of spastic muscles by Tolserol therapy is discussed This and other methods of treating patients suffering from *spondylitis* are described

The perspective of a single specialist is apt to be limited, the most recent advances in all fields can seldom be familiar to the general practitioner The most complete care for the patient comes from a wise practitioner supplemented by the combined and integrated consultations of specialists In this symposium on acute medical emergencies the chiefs and their assistants in the respective specialties of the Medical Division of this Clinic have aimed at the simplification of diagnosis and therapy, have warned of hazards and stressed prophylactic measures In so doing they have dedicated this symposium to those physicians on whom rests so much of the responsibility for the early diagnosis and proper subsequent care of the sick—the general practitioner

GARFIELD G DUNCAN, M.D

THE RECOGNITION AND EMERGENCY TREATMENT OF VENOUS THROMBOSIS AND ITS COMPLICATIONS

DAVID S. MARSHALL, II, M D *

Were it not for the frequency with which pulmonary embolism has its source in venous thrombosis, the subject of thrombophlebitis and phlebothrombosis would scarcely deserve consideration in a clinic on medical emergencies Although Virchow, as early as 1846, first described the relationship between embolism to the lung and venous thrombosis elsewhere in the body, it has not been until the last decade that active therapeutic measures have been undertaken to avert the tragedy of pulmonary embolization The purpose of this paper is to discuss the clinical recognition of venous thrombosis, and to suggest methods of management with particular reference to anticoagulant therapy

VENOUS THROMBOSIS

Venous thrombosis usually occurs as a furtive process termed by Ochsner as "phlebothrombosis."[1] It may arise in any segment of the venous tree although evidence suggests over 90 per cent originates in plantar or soleus veins of the leg[2, 3] If one reflects on obvious limitations of venous exploration at necropsy, the evidence must be viewed with question Initially a soft thrombus shapes on an agglutinated layer of platelets in a small vein of the muscle Propagating toward the heart, this clot soon invades major venous channels Thus, with brittle anchorage in a small calf vein, a nonadherent clot may extend high into the femoral vein The proximal end agitates freely in the surrounding venous stream Clinical manifestations may be absent With a patient's activity, alterations of the venous pressure threaten clot detachment and pulmonary embolization

When the developing thrombus enlarges and completely occludes the lumen, it slowly becomes adherent to the endothelium The muscle segment drained by the vein then becomes edematous The skin may present a more glossy appearance over the involved muscle Palpation yields a firmer calf muscle consistency If mild inflammation occurs where the clot first developed, the patient sometimes complains of a faint ache, cramp, or "drawing" sensation Localized tenderness close to the vein may be present Little circulatory disturbance or inflammation is present early A massive fatal pulmonary embolus may be the first indication of the process

With progressive occlusion of major veins and tributaries signs and symptoms of venous occlusion and inflammatory reaction are more evident Inspection may reveal appreciable calf swelling an accentuated

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superficial venous pattern, or faint cyanosis Palpation reveals increased warmth and greater tenderness Homans' dorsiflexion sign is sometimes present early The sign consists of calf pain elicited by forceful but not traumatic dorsiflexion of the foot, with the leg extended A slight fever and leukocytosis sometimes occur

As the clot progresses and adheres to the endothelium of the popliteal, femoral and iliac veins, more severe pain may occur. Redness of the skin, particularly along the course of the involved vein, sometimes is evident. Edema is usually augmented by perivenous lymphatic involvement secondary to periphlebitis, and an overtaxed superficial collateral circulation Tenderness may be elicited by calf compression, palpation along the course of the popliteal and femoral veins, at the femoral tri-

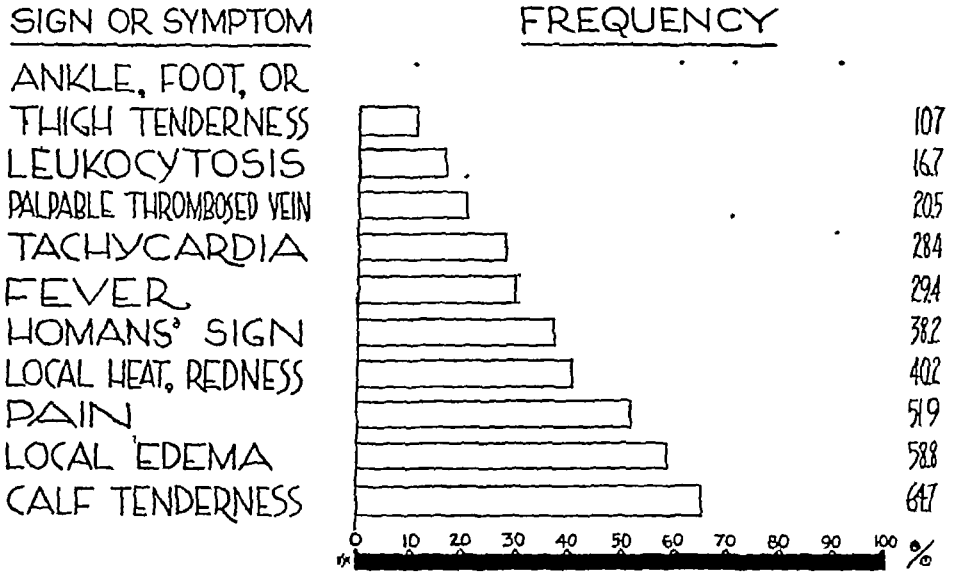

Fig 255 —Percentage analysis of signs and symptoms in a series of patients with venous thrombosis as observed in the Pennsylvania Hospital

angle, or in the lower abdomen Occasionally a palpable clot lies in the femoral vein Pulsations of the adjacent femoral artery are commonly weaker General systemic signs and symptoms are exaggerated Reflex vasospasm associated with this extensive process sometimes simulates embolic arterial occlusion The presence of cyanosis of the extremity rather than pallor immediately following the onset is evidence for vasospasm with venous thrombosis Pulses are imperceptible, and the affected part becomes cool The term *acute thrombophlebitis* is applied to this syndrome

With the adherence of the thrombus to the endothelium, organization of the clot ensues This is complete in three or four weeks with endothelialization of the exposed surfaces Only then is the immediate danger of embolization ended.

From this discussion, the gradations of venous thrombotic disease between phlebothrombosis and thrombophlebitis are evident The signs and symptoms vary depending on the pathological phase (Fig 255) Necropsy reports suggest that phlebitis is found in 15 per cent of patients with venous thrombosis [2] Clinical evidence for phlebitis does not exclude the presence of a soft loose clot in a vein proximal to the phlebitic area Fine and Starr describe three cases of acute thrombophlebitis in which large nonadherent proximal thrombi were aspirated from the iliac veins at operation [4]

The syndrome of *pelvic vein thrombosis*, involving the broad ligament, periprostatic or periurethral areas, has been described It is of interest in inflammatory pelvic or genitourinary disease Pain and swelling in the gluteal or adductor muscles, sciatic neuritis, mucous diarrhoea, and slight suprapubic edema may occur Palpable cords lateral to the uterus or prostate are diagnostic aids

Thrombosis in the *superficial saphenous system* should lead one to suspect deep venous thrombosis In a study on fifty-one cases of fatal postoperative pulmonary emboli, thirty of this group revealed lesser saphenous involvement [5] The fatal emboli probably arose from detached asymptomatic thrombi in the femoral or iliac veins

Venous thrombosis in the *upper extremities* is infrequently recognized The signs and symptoms correspond to those of the lower extremities We have seen two cases of brachial thrombophlebitis on the medical service in the past thirty months Both were patients with congestive heart failure One died with multiple pulmonary emboli contributing to her death

PULMONARY EMBOLISM

In 40 per cent of patients with deep venous thrombosis, the first evidence may be signs and symptoms of pulmonary embolism [6, 7] Approximately four of each ten patients with pulmonary embolism will die before therapy can be started [8] If untreated, 32 per cent or more of the survivors will die later because of multiple embolic episodes in most instances [8, 9] The signs and symptoms vary (Fig 250) depending on (1) the size of the embolus, (2) the location of the embolus, (3) the antecedent health of the lung, (4) the extent of central thrombotic propagation from the initial lesion, and (5) whether or not infarction of the lung occurs

Over 90 per cent of the emboli involve the right or left lower lobe [7] Minimal diagnostic clues often suggest a small embolus Lodging close to the lung periphery, the embolus may elicit a pleuritic response The patient experiences a "stitch" in the chest, or actual pleuritic pain Unexplained concurrent tachycardia and low grade fever are important suggestive findings. Physical signs are usually absent Occasionally a pleural friction rub is heard

Large emboli will produce more severe symptoms The cumulative effect of numerous small emboli may do likewise Pain occurs, often

suggestive of myocardial infarction The restless patient may appear ashen or cyanotic Dyspnea is usual Vomiting sometimes occurs Syncope, unconsciousness, convulsions or shock may ensue Increased fever, tachycardia and feeble pulse are common The lung fields may reveal no immediate abnormal findings With occlusion of large vessels, pulmonary hypertension occurs The second pulmonic sound is accentuated, and the heart is rapid Some patients develop a diastolic murmur in the mitral area In a recent patient, we observed a friction rub localized in the pulmonic area which disappeared within thirty-six hours If right ventricular dilatation and failure occurs, the patient may die of cardiac insufficiency within several hours or days

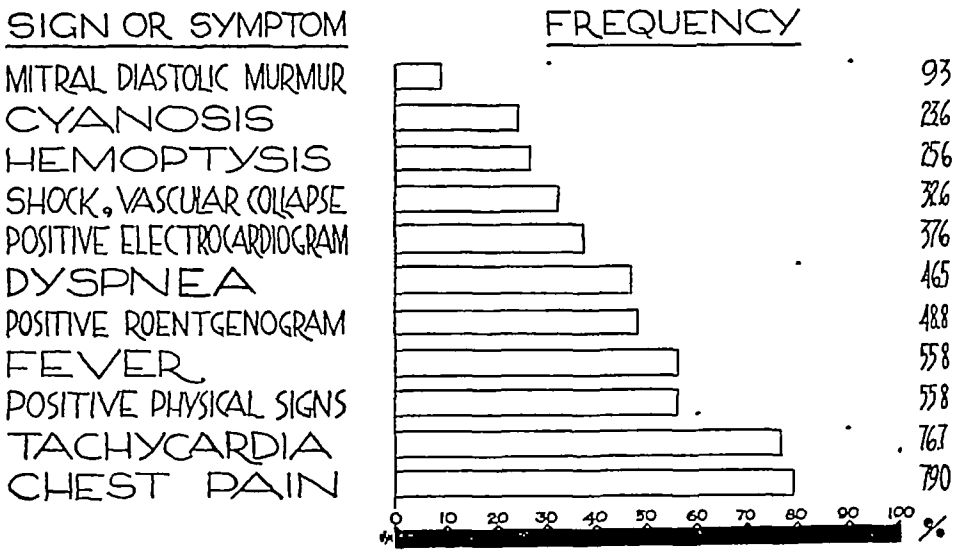

Fig 256 —Percentage analysis of signs and symptoms in a series of patients with pulmonary embolism as observed in the Pennsylvania Hospital

With exudation of fluid following pulmonary stasis and vessel wall damage, crepitant rales are commonly heard Further pulmonary findings depend on two possible pathological trends First, occurring oftener in a previously healthy lung, a period of local ischemia occurs in the involved area Collateral circulation by the bronchial arteries may take place with subsequent resolution Secondly, if extensive fluid exudation or a hemorrhagic lesion occurs, bronchial obstruction and atelectasis of the involved pulmonary segment develops Classical signs and symptoms of atelectasis are followed shortly by those of pneumonic solidification Hemoptysis is rare With either course, widespread pleural involvement may develop when the infarcted area extends to the lung periphery Local percussion tenderness and pleural friction rub may occur Pleural effusion sometimes develops With diaphragmatic pleura involvement, upper abdominal rigidity may suggest a surgical abdomen

DIAGNOSTIC AIDS FOR VENOUS THROMBOSIS AND PULMONARY EMBOLISM

Phlebography—Recommended enthusiastically by Bauer,[3, 10] we have found, as others, that venography is undependable[1, 11] Variations in the deep venous patterns of normal individuals make interpretations of the abnormal difficult[12] Allen reports negative venograms in 33 per cent of patients with clinical venous thrombosis, negative studies in 50 7 per cent of patients with pulmonary emboli, and 41 per cent positive films in a group with negative clinical findings[7] Other objections are that it is expensive, it involves movement of the patient when motion may precipitate a pulmonary embolus, it is often an uncomfortable procedure, and the 35 per cent diodrast solution used as a contrast medium may produce thrombosis in distorted veins with slow circulation

Chest Roentgenography—For patients with pulmonary embolism, we have found chest films valuable but often disappointing Both oblique and anterior views are desirable[13] Findings are variable With small emboli, the film may be negative or haziness may be seen in the infarcted area due to adjacent inflammation or pleurisy Larger infarcts produce areas of decreased or absent vascularization, due to ischemia distal to the embolus Wedge-shaped areas of infarction are infrequently observed Consolidation may not be seen for twenty-four hours after embolization Unfortunately when shadows of atelectasis, pleural effusion or pneumonia appear, pulmonary embolism is frequently ignored as a source

Electrocardiography—The classical pattern of acute right ventricular strain is not often seen on the electrocardiogram of a patient with pulmonary embolism This pattern consists of a deep S_1 and Q_3, a transient intraventricular conduction delay, RS-T segment depression in the first limb lead and elevation in the third, inversion of T_3, or T_2 and T_3, and inversion of the T wave in the second precordial lead[14] Not uncommon are tracings suggesting acute coronary insufficiency[15] These shows RS T segment depressions in the limb and precordial leads with associated T wave flattening or inversion in one or many leads A transitory right axis shift may occur, and unipolar leads may give evidence for clockwise rotation of the heart on the long axis Sinus tachycardia is common, and occasionally tachycardias originating from ectopic foci are seen Malinow has demonstrated that the electrocardiographic changes are not related to a pulmonocoronary reflex[16] Because of the rapidity with which the electrocardiographic changes associated with pulmonary embolism may return toward normal, it is imperative to obtain a tracing as quickly as possible when the condition is suspected The abnormal findings may disappear within a few hours and, in these cases, several comparative records are of the greatest diagnostic value. The greater the delay in obtaining electrocardiograms, the less likely are they to be of value as a diagnostic aid

PROPHYLACTIC TREATMENT FOR VENOUS THROMBOSIS AND PULMONARY EMBOLISM

The therapeutic approach to venous thrombosis must be concerned with prophylaxis as well as specific treatment, otherwise, many pulmonary emboli cannot be averted Venous thrombosis by its nature implies alterations of the normal clotting mechanism The factors responsible are incompletely understood If a convenient, reliable test were available for determining an increased clotting tendency, the problem of prophylaxis might be simplified At present, no such test is available

Prophylactic measures may be specific or nonspecific Specific measures are directed toward the clotting mechanism proper, altering it in a manner to prevent intravascular thrombosis irrespective of location For this purpose two clinically proven drugs, heparin and Dicumarol, are available Nonspecific methods, directed toward other than the clotting mechanism, include surgical ligation and procedures minimizing venous stasis

Choice of Patients.—It is practically and economically impossible to institute prophylactic therapy in all patients A choice must necessarily be made of patients predisposed to the development of venous thrombosis These include

1 Patients over 40 years of age, particularly in the fifth and sixth decades, who are bedfast for medical or surgical reasons [7, 17, 18, 19]
2 Obese patients who develop venous thrombosis twice as often as patients of normal weight [19]
3 Patients with a previous history of venous thrombosis or who have varicose veins [19 20 21]
4 Medical patients who are more susceptible than surgical patients with a frequency of 2 1 per cent among all cases, and a 19 per cent mortality among untreated patients [2 22] Particularly predisposed are patients with
   (*a*) Cardiac disease Noteworthy are those in congestive failure or with myocardial infarction [19 23, 24] Pulmonary embolism mortality increases strikingly if complicating congestive failure [17 18]
   (*b*) Prolonged febrile illnesses These include scarlet fever, subacute bacterial endocarditis, atypical virus pneumonia, typhoid fever, scrub typhus, and infectious mononucleosis [24 25 26]
   (*c*) Malignant diseases Of particular concern are leukemia, polycythemia vera, and neoplasms of the colon, rectum and brain [19]
5 Postoperative patients who have a 1 61 per cent frequency [2] If untreated, the mortality is 16 6 per cent [2] Surgery of the uterus, hernias, the extremities, the bladder and the perineum is most apt to produce venous thrombosis [23 12]
6 Postpartum patients who reveal venous thrombosis in 1 2 per cent of all cases The mortality among untreated patients is 3 6 per cent [2]
7 Patients with traumatic injuries, particularly elderly patients with hip fractures [2 12 18 25 27]

General Prophylactic Measures.—These measures are directed toward minimizing various factors, such as venous stasis and trauma, which [illegible] believed to be of importance in initiating intravascular clotting [illegible] are the following precautions

1 Avoid infections
2 Avoid trauma. This includes surgical trauma
   (a) Protect wound edges
   (b) Insert abdominal and pelvic retractors with care.
   (c) Handle tissues gently
   (d) Careful hemostasis
3 Avoid absolute bed rest when feasible.
   (a) Early postoperative and postpartum ambulation
   (b) Exercise of extremities while in bed
   (c) Prohibit elderly patients from sitting on the bed with their legs hanging over the edge
   (d) Ambulation preoperatively when possible.
4 Deep breathing exercises in bed Use carbon dioxide inhalation if necessary
5 Fifteen degree elevation of foot of bed for bedfast patients
6 Weight reduction of the obese
7 In patients with varicose veins
   (a) Use of elastic stockings or bandages
   (b) Treatment of varicosities by surgery or injection
8 Correction of cardiac failure.
9 Maintenance of proper nutrition

These measures have wide applicability and the expense is minimal Many of the precautions are of controversial merit and one has little assurance that venous thrombosis and pulmonary embolism will not occur

Prophylactic Femoral Ligation —The rationale of this method is based on the supposed frequency of venous thrombosis originating in the lower leg It protects against pulmonary emboli arising from venous thrombosis developing distal to the point of ligation It does not protect against the development of venous thrombosis, or emboli from such a source proximal to ligation The procedure has decreased the incidence of fatal embolic disease in postoperative patients to 4 per cent of that seen in a similar control group, and the incidence of postoperative phlebitis to 9 per cent of that in a control group [28, 29] The operation is simple with little or no mortality risk It should be done bilaterally, for one cannot predict the leg potentially involved *We feel the procedure should be reserved for patients in whom anticoagulant therapy is contra indicated*

Prophylactic Anticoagulant Therapy —As a specific prophylactic measure, anticoagulant therapy using heparin or Dicumarol has distinct merit These drugs protect against intravascular thrombosis in all parts of the vascular tree The reports on heparin or Dicumarol used as prophylactic drugs reveal statistical results equal or better than those of vein interruption In 400 postoperative patients comprised of groups representing the highest incidence of thrombosis and pulmonary embolism, Murray instituted prophylactic heparin therapy No patient developed venous thrombosis or pulmonary embolism [30] Barker and others gave Dicumarol for prophylaxis in 1302 postoperative patients None developed pulmonary embolism, and only two developed minimal venous thrombosis [31] However, there are limitations to the use of anti-

coagulants Dicumarol cannot be safely used without daily prothrombin time determinations upon which the daily dose rests The risk of hemorrhage with either drug is minimal only with proper dosage schedules

Definite *contraindications* to anticoagulant therapy exist and, if violated, an added risk of hemorrhagic complications occurs Conditions which contraindicate are

1 Diminution of the normal prothrombin activity of plasma, as in hepatic disease or ascorbic acid and vitamin K deficiencies
2 All types of purpura and hemorrhagic blood dyscrasias
3 Recent surgery on the brain or spinal cord Minimal hemorrhage here may be disastrous
4 Recent cerebrovascular accidents
5 Ulcerative lesions and open wounds
6 Subacute bacterial endocarditis
7 Decreased kidney function

The time to start prophylactic administration of anticoagulants depends on whether the patient is a surgical or medical problem If ample time is allowed prior to the surgical procedure so that the prothrombin time and coagulation time may be restored to normal, the drugs can be given preoperatively if indicated Heparin is more ideally suited to this purpose as the effect can be neutralized immediately when necessary In general, bedfast patients are most apt to develop venous thrombosis from the third to twenty-first days of bedrest Unless contraindicated, therapy may be started on the first day in medical patients In uncomplicated postoperative and postpartum patients, Dicumarol therapy may be started on the second day after delivery or operation Because of its slow anticoagulant effect, there is small danger of hemorrhage at the operative site The drug has no effect on infants nursing from treated mothers [21] We routinely reserve the use of heparin for patients in whom an immediate anticoagulant effect is desirable It is difficult to use for prolonged prophylaxis and is expensive Under any circumstance, we hesitate to use the drug before the third or fourth postoperative or postpartum day

DeTakats reports the prophylactic use of prostigmine and sodium tetrathionate after laparotomies [25] The action of the drugs on the clotting mechanism is uncertain No patient among several hundred developed thromboembolic complications

THE TREATMENT OF VENOUS THROMBOSIS AND PULMONARY EMBOLISM

If the mortality rate associated with venous thrombosis is to be significantly altered, it is the obligation of the physician to institute treatment upon the earliest suggestive symptom or sign of its presence A valuable maxim is to treat when in doubt Patients with venous thrombosis or pulmonary embolism may be treated surgically or medically A variety of surgical procedures involving ligation of venous channels has been used We feel they are of value in patients who are poor anticoagulant therapy risks

Low Venous Ligation.—This includes superficial femoral or common femoral vein ligation

Superficial femoral ligation usually includes phlebotomy, thrombectomy and surgical interruption of the vein It should never be done unilaterally as there is a 30 per cent probability that thrombosis is present or will arise in the opposite leg [2] It is not to be done in the presence of a tender swollen groin or thigh It is used for thrombosis, with or without pulmonary embolism, which is confined to the lower leg Results are good Among 1300 superficial and common femoral ligations reported by Allen and others, only three deaths occurred following superficial femoral ligation, all three had one or more pulmonary emboli prior to ligation [29]

Common femoral ligation, an unpopular procedure among surgeons, is sometimes associated with profound shock [30] The vein is short and cannot be divided easily If a lymphatic area is entered, damage to lymph channels may occur Collateral circulation is poor with ligation at this point, and troublesome edema may follow [31] The procedure was designed to protect from emboli arising in the deep femoral vein Higher ligations are favored over this method

High Venous Ligation —This includes common iliac and inferior vena caval ligations Indications are for high femoral thrombosis, iliac thrombosis, or higher involvement It is done for pulmonary embolism with no evidence of venous thrombosis in the extremities General anesthesia is necessary because of the hazard of precipitating a pulmonary embolus while positioning the patient for spinal anesthesia [21] The procedures are major but not formidable

Common iliac ligation, a more complex procedure than inferior vena cava ligation, should be done bilaterally The danger of hemorrhage exists in freeing the vein from adjacent tissues and the iliac artery A more satisfactory collateral circulation occurs than with common femoral ligation

Inferior vena cava ligation may be done by an extraperitoneal or abdominal approach With pelvic or uterine vein thrombosis, the abdominal approach must be used to permit ligation of the ovarian veins If the thrombotic process arises from the legs, the extraperitoneal approach is of merit This ligation allows extensive collateral circulation It is a less involved surgical procedure, and because it gives the increased security of higher ligation, vena caval ligation is preferable to bilateral iliac vein interruption

Anticoagulant Therapy —We feel that the combined use of heparin and Dicumarol is indicated for venous thrombosis or pulmonary embolism The reasons are (1) Parenteral heparin produces a prompt anticoagulant effect It acts with a plasma co-factor to prevent conversion of prothrombin to thrombin, with serum albumin, it forms an antithrombin, and it prevents the formation of thromboplastin from platelets [32] Changes in the electrical properties of proteins may be important in its action [33] It acts on clots regardless of site or stage Loewe has furnished evidence that dissolution of unorganized clots occurs with its

use [12] Bauer demonstrated prompt arrest of thrombotic processes [2] Although the drug acts promptly, the effect is fleeting Its effect is measured by the prolongation of the *whole blood coagulation time* It is an expensive drug for prolonged use (2) Oral Dicumarol produces a delayed anticoagulant effect, and may be ineffective within twenty-four to thirty-six hours of administration It acts by depressing the liver production of an essential clotting factor, prothrombin, thus indirectly altering the clotting mechanism proper [38] The effect is measured by its prolongation of the *plasma prothrombin time* With large doses, prolongation of the clotting time may be demonstrated but this action is not significant as determined by present laboratory technics [34] The effect of a dose of Dicumarol is prolonged over several days

Thus, the combined use of heparin for its *immediate* effect, and Dicumarol for its delayed but *prolonged* effect seems rational When the diagnosis of venous thrombosis or pulmonary embolism is made, heparin and Dicumarol should be administered without delay

METHODS OF ADMINISTRATION —*Heparin* —Methods of administering this drug are many and varied Statistics give evidence that each method gives comparable clinical results

1 Intravenous heparin by continuous drip [30] Using 200 mg of heparin in 1000 cc of saline, glucose solution or distilled water, an intravenous infusion is started at 30 drops per minute Rate of flow is adjusted to maintain clotting time between thirty and forty-five minutes Clotting times are determined at least twice daily The method is difficult to maintain for long periods, and there are inherent dangers in alterations of the rate of dropping

2 Intravenous heparin by intermittent dosage [8, 2] Popularized by the Swedish school, this method is used almost exclusively at this institution We administer intravenous injections of 50 mg of heparin solution, 10 mg /cc , at four to six hour intervals Clotting times are not essential as the danger of hemorrhage on this program is remote We routinely do a control clotting time and another prior to the second dose to exclude hyperactivity The anticoagulant effect of each dose lasts for but a few hours However, the results are comparable to continuous heparin methods It is a less difficult and less dangerous mode of administration Heparin is continued until the Dicumarol, administered daily coincident with heparin therapy, produces a prothrombin time within therapeutic levels

3 Deep subcutaneous or superficial intramuscular injection of heparin in Pitkin menstruum [12] Three hundred milligrams of heparin incorporated in Pitkin menstruum (gelatin, dextrose, glacial acetic acid and distilled water) are injected as a single dose The anticoagulant effect is more delayed than with intravenous heparin, but the effect is prolonged One injection usually suffices for forty-eight hours Coagulation times are done before the first dose and daily Loewe suggests a coagulation time not less than three times the normal be maintained [12] The drug is injected in the anterior or lateral aspect of the thigh It is sometimes painful, even with the new rebuffered preparations

4 Intermittent subcutaneous injection of the sodium salt of heparin.[19 35] Heparin is given in 30 mg doses by subcutaneous injection every three hours Clotting times are determined once or twice daily, and clotting times of three times the normal are desired It may be given by persons incapable of skilled venopuncture.

5 Intermittent intramuscular injection of concentrated aqueous heparin [36] A concentrated solution of heparin, 100 mg /cc , is used in contrast to the available commercial solutions containing 10 mg per milliliter Adequate prolongation of the clotting time is obtained with 100 mg intramuscularly every eight hours for patients weighing from 100 to 130 pounds, and 120 to 140 mg every twelve hours for patients from 120 to 140 pounds The maximum daily dose is 450 mg It is recommended that the coagulation time be determined daily before the dose The effect of a dose occurs in thirty to sixty minutes, and is maximum in four to six hours The results are the same as with other methods Clinically, we are not familiar with this technic

Dicumarol (3,3 methylene-bis[4-hydroxy]coumarin) —The oral dosage schedules are variable in the literature [21 37] The following plan, which we use, is safe and effective In this hospital a single team is responsible for Dicumarol administration on all services

1 A control prothrombin time is determined prior to the first dose The blood is drawn prior to the intravenous dose of heparin or three hours afterwards as heparin interferes with the prothrombin time [38] By the technic employed in this hospital, a normal control prothrombin time varies between 13 and 17 seconds

2 An initial dose of 300 mg is given The dose on successive days is thereafter determined by the daily prothrombin time of the patient (Fig 257)

3 A dose of 300 mg is given daily until the prothrombin time is 30 seconds

4 Either 200 or 100 mg are given daily when the prothrombin time is within the range of 30 to 35 seconds

5 If the prothrombin time exceeds 35 seconds, no Dicumarol is given until the daily prothrombin time falls below 35 seconds The ideal therapeutic range is between 30 and 50 seconds

6 The daily doses are given on the above schedule If a patient is hyperreactive to the drug, doses of 50 mg may be necessary to maintain the therapeutic level

7 If the prothrombin time exceeds one minute, we routinely administer parenteral vitamin K to control the excessive rise If the rise occurred slowly, the drug is given intramuscularly in 4 8 mg doses every four hours until the prothrombin time is within therapeutic limits Intravenous vitamin K is given in 72 mg doses, if the rise has been very rapid, and continued at twenty four hour intervals until the therapeutic zone is restored

8 If gross hemorrhage occurs, it is controlled by fresh whole blood and vitamin K as outlined below

LABORATORY CONTROL — *Heparin* — The anticoagulant effect of heparin is determined by the Lee-White method of determining blood coagulation time Although this method is crude, it is adequate for the safe administration of heparin In our laboratory the normal range is from eight to fourteen minutes With heparin therapy by the intermittent

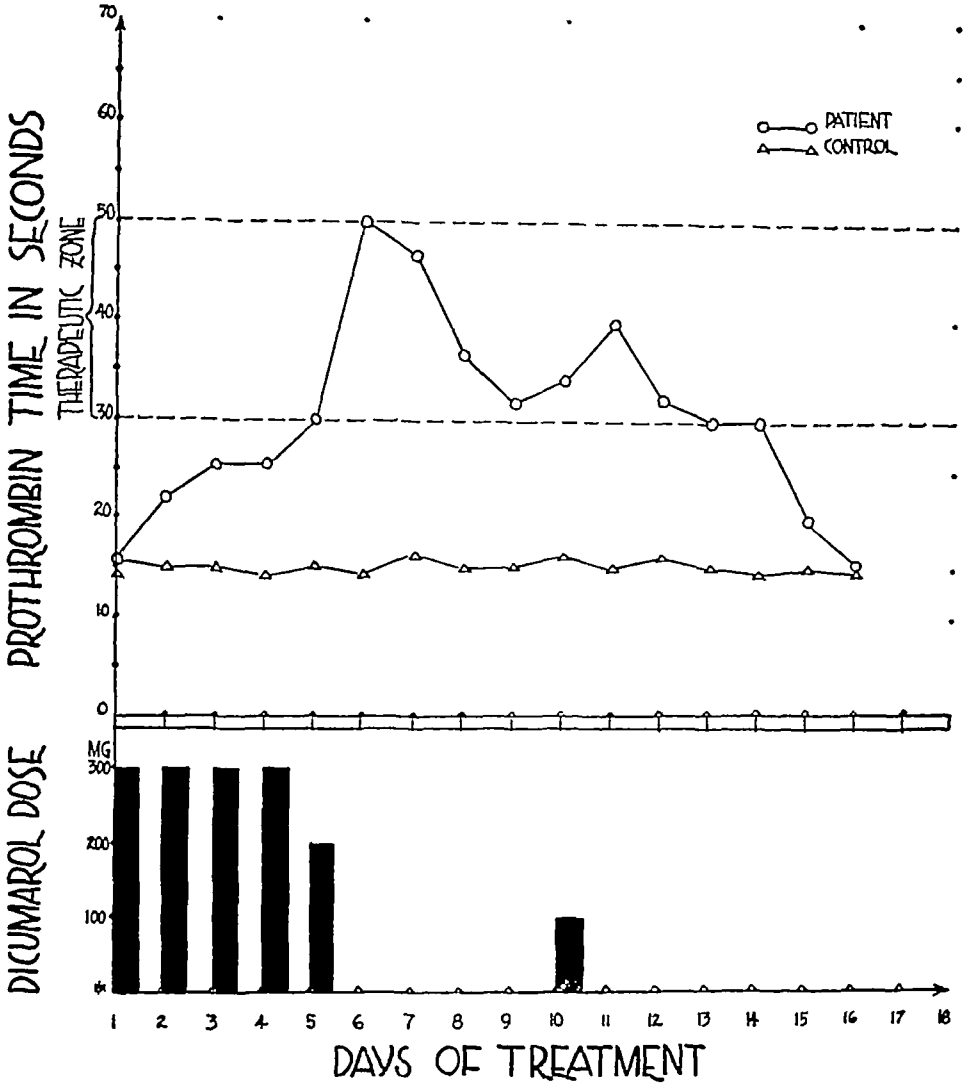

Fig 257 — A graph showing the delayed but prolonged anticoagulant action of dicumarol The daily dose depends upon the daily prothrombin time determination

intravenous technic, the coagulation time may be prolonged for over one hour within ten minutes of the injection (Fig 258) It drops sharply, however, and within four to six hours has returned toward normal The short duration of the peak effect probably is responsible for the absence of hemorrhage With peaks maintained above one hour for long periods, the danger of hemorrhage increases If the coagulation time has not

returned toward normal within four hours, the next dose is delayed until such has occurred

Dicumarol—The anticoagulant effect of Dicumarol is measured in our laboratory by the Link-Shapiro modification of Quick's technic[3] This method utilizes undilute plasma It is advantageous over the dilute plasma technic in that it is less time-consuming and the errors in technic are less exaggerated The details of the procedure are available else-

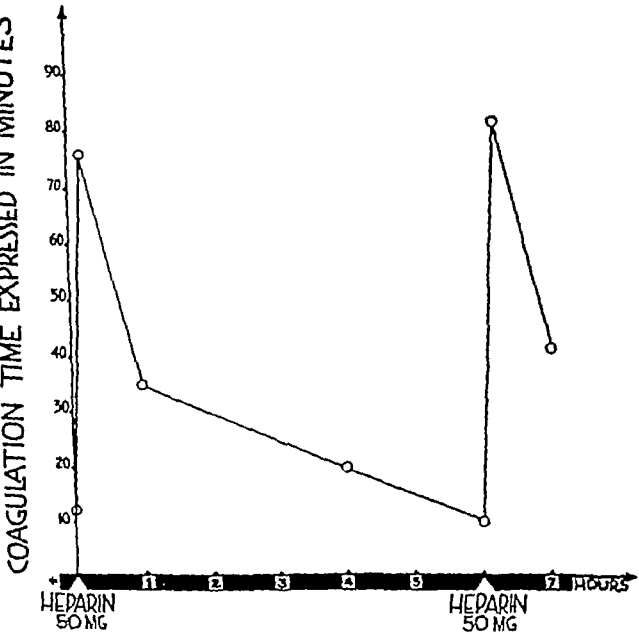

Fig 258—A graph showing the immediate but transient anticoagulant effect of heparin as given by the intermittent intravenous method

where. Although a relatively new standard laboratory procedure, the test is less complex than many established routine laboratory studies We use a commercial thromboplastin preparation which we have usually found to be of *constant potency* The daily prothrombin time of the patient receiving Dicumarol is compared to a daily prothrombin time determined on a plasma with known normal prothrombin activity Rather than drawing blood from a presumably normal patient daily to serve as a control we find banked plasma of known normal prothrombin

activity is useful and convenient A fresh plasma sample is chosen with a prothrombin time between thirteen and fifteen seconds Five milliliter quantities are distributed equally into test tubes, rubber capped, and placed in the deep freeze unit One tube is withdrawn daily to serve as a control This constant control specimen aids as a check on the potency of the thromboplastin-calcium solution Because of a human error element in determining the end point of the test, more uniform readings are obtained if one technician is assigned to the procedure A stop-watch with foot-pedal control will further decrease this error

With daily normal controls between 13 and 17 seconds by our laboratory technic, we endeavor to keep the daily prothrombin time of the treated patient between 30 and 50 seconds This is considered an optimum range, beyond which hemorrhage is apt to occur, and below which further thrombotic progression is likely to occur

CONTROL OF HEMORRHAGE —*Heparin* —Should hemorrhage occur, the drug is stopped Immediate neutralization of the heparin effect may obtained by giving protamine sulfate solution, 1 or 2 per cent, intravenously The dose is computed on the belief that 1 mg of heparin is neutralized by 1 or 2 mg of protamine sulfate Blood transfusions are useful to replace blood loss, and for a gradual restoration of clotting time to normal

Dicumarol —Gross hemorrhage with Dicumarol therapy is not so easily controlled The incidence of major hemorrhage in a group of 1686 postoperative patients receiving Dicumarol was 1 9 per cent as reported by Allen [40] Minor hemorrhage occurred in 3 1 per cent With major hemorrhage, the drug is discontinued Fresh whole blood transfusions give a rapid effect decreasing the hypoprothrombinemia for several hours Synthetic vitamin K (Hykinone), 72 mg , is given intravenously at four hour intervals until bleeding ceases The drug reduces the prothrombin time to safe limits within twelve to forty-eight hours Reconstituted lyophilized plasma, 500 cc , reduces the prothrombin time from high to safe levels quickly and the effect is maintained six to ten hours With minor hemorrhage, such as epistaxis or microscopic hematuria, the Dicumarol is stopped until hemorrhage ceases, and then continued with lower doses

DURATION OF THERAPY —We routinely continue anticoagulant therapy until the patient is ambulatory for several days to a week It is continued in bedfast patients although evidence suggesting thrombosis has disappeared Ambulation is allowed, unless other conditions contraindicate, when signs and symptoms of the acute process have subsided and the temperature returns to normal An average course is seven to fourteen days

Miscellaneous Therapeutic Procedures.—1 Elevation of the extremities to facilitate venous return flow

2 Complete bed rest until the process becomes quiescent

3 Avoidance of coughing, straining at stool and deep breathing Such activity may precipitate a pulmonary embolus

4 Application of heat to the extremity The extremity is coated with petrolatum to prevent skin maceration Moist hot packs are applied about the leg, covered with rubber matting, and surrounded by hot water bags These are applied continuously except for a daily four hour period to allow drying of the skin The rationale is to allay vasospasm and pain

5 Intravenous procaine is used to arrest vasospasm associated with acute thrombophlebitis A solution containing 500 mg of procaine in 500 cc of normal saline solution is given intravenously by slow drip, starting at the rate of 15 drops per minute It is continued until relief is obtained Convulsions or a precipitous drop in blood pressure may occur With convulsions, the drug is discontinued and sodium pentothal is given slowly intravenously until the convulsions are controlled The drug should be kept at hand for emergency usage If a rapid drop in blood pressure occurs, the drug is discontinued and 0.2 mg of neosynephrine or a test dose of desoxyephedrine, 5 mg , is given intravenously The dose of desoxyephedrine should never exceed 10 mg

6 Paravertebral lumbar sympathetic block This involves blocking the first to fourth lumbar ganglia inclusive with a 1 per cent procaine solution, As with intravenous procaine, it is used to relieve severe phlebitic pain resulting from arterial spasm and to restore arterial circulation Because of the short duration of the procaine effect, it is sometimes necessary to repeat the injection every three or four hours Either type procaine therapy seldom needs to be used Neither procedure should be used alone in the treatment of thrombophlebitis

7 Smoking is prohibited

Therapeutic Measures for Pulmonary Embolism.—The success of therapy in pulmonary embolism depends largely on the rapidity of application A suggested plan of management follows

1 Immediate treatment
   (a) Oxygen by catheter or mask with the patient propped to a semisitting position
   (b) Injection of 50 mg of heparin intravenously and continuance of the anticoagulant program of heparin and Dicumarol as outlined above
   (c) Atropine sulfate, papaverine hydrochloride and morphine are of controversial and doubtful value
2 Later management
   (a) If right ventricular failure should occur, digitalis is of uncertain value Some believe it is contraindicated
   (b) If severe pleuritic pain occurs, procaine block of the overlying intercostal nerves may be useful
   (c) Ambulation is permitted when clinical signs and symptoms have disappeared and the anticoagulant effect is within the therapeutic range

SEQUELAE OF VENOUS THROMBOSIS

The sequelae of venous thrombosis are related to venous incompetency With obstruction of the deep veins, the collateral subcutaneous

venous channels must take over their function There is roentgenological evidence that recannalization of the deep veins almost never occurs [2] If the load is excessive, the superficial venous channels become tortuous, distended, and develop valvular incompetency With incompetency, edema occurs Thrombophlebitic edema fluid is rich in protein which coagulates to produce a fibroblastic reaction and irreversible damage Fibrosis and ulceration are not uncommon Bauer believes the so-called varicose ulcer should be termed the "post-thrombotic ulcer".[2] He found 80 to 90 per cent of his patients had varices related to earlier deep thrombosis Indurative skin lesions occur which are, in some instances, the result of localized increased allergic sensitivity [41]

Measures used in the treatment of sequelae are:

1 The continued use of elastic bandages from the foot to the knee or higher is indicated for edema Patients should avoid standing for long periods, particularly during hot weather

2 If pain occurs with activity, rest or a cool tub bath generally give relief If muscle cramps occur at rest, a single dose of quinine, 0 33 gm (5 grains), is often rapidly effective.

3 Radical surgical excision of ulcers followed by split-thickness skin grafts may be of value Edema of severe degree may break down the graft

4 Chronic recurrent and migratory phlebitis may be interrupted with a four week course of anticoagulants [35]

SUMMARY

1 The signs and symptoms of venous thrombosis and pulmonary embolism are discussed From a therapeutic viewpoint, both phlebothrombosis and thrombophlebitis must be considered as medical emergencies

2 Phlebography, chest roentgenography and electrocardiography are sometimes of aid in the diagnosis of venous thrombosis and pulmonary embolism

3 Prophylactic therapy is necessary to decrease the incidence of pulmonary embolism as the first manifestation of venous thrombosis Patients susceptible to venous thrombosis are discussed, and the available methods of treatment We believe surgical prophylactic procedures are indicated only if anticoagulant therapy is contraindicated

4. If a doubt exists that venous thrombosis or pulmonary embolism may be present in a patient, we believe that the patient should be given the benefit of the doubt and be treated with anticoagulants

5 The available surgical, medical and general methods of treatment for venous thrombosis or pulmonary embolism are outlined

6 The anticoagulants, heparin and Dicumarol, are discussed The various methods of administration, programs of management, and labora- control are emphasized We believe the combined use of heparin icumarol is most rational in respect to their pharmacological es methods of administration, and for economic reasons

7 The sequelae of venous thrombosis which may cause chronic disability are briefly remarked upon

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THE TREATMENT OF ACUTE CARDIOVASCULAR CONDITIONS

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Cardiovascular emergencies are an important part of general medical practice Various episodes affecting the cardiovascular system may or may not demand emergency measures The general condition of the patient, the circumstances under which the incident occurs, and the severity of the condition itself may be operative in determining whether or not the situation represents an emergency Of the numerous affections which involve the vascular system, certain are more frequent and important than others An attempt has been made to include the salient features of diagnosis and treatment of these conditions

SYNCOPE

Syncope may result from a variety of causes and constitutes an important cardiovascular emergency The prognosis varies greatly with the cause of the attack Benign syncope, or a simple fainting spell, is a relatively harmless affair, but, when syncope results from such conditions as ventricular fibrillation, the attack may be fatal Satisfactory therapy depends on a correct diagnosis and in most instances a good idea of the cause may be obtained from the history and clinical examination Conditions which may cause syncope, besides the common fainting attack, are Adams-Stokes syndrome, the onset of very rapid tachycardia, carotid sinus syncope, and rare causes such as attacks of transient ventricular fibrillation

Benign Syncope —This condition usually occurs in the absence of organic heart disease Certain individuals are prone to fainting attacks during much of their life, even though they may be otherwise healthy The attack itself is apt to be precipitated by the sight of blood, anticipation of a medical procedure or similar circumstances In such persons, sudden changes of position, especially if the person has been lying flat or standing motionless for a long period, are predisposing factors The mechanism of the attack is usually a sudden vagal outflow associated with marked slowing of the heart and a drop in blood pressure In a patient we observed during an attack of syncope, while taking an electrocardiogram, there was a sudden slowing of the auricular rate, followed by complete arrest of both auricles and ventricles for a period of several seconds

In the treatment of benign syncope, prophylactic therapy is seldom of value, although such drugs as atropine and ephedrine may be tried

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in susceptible persons who exhibit a sinus bradycardia If an individual appears faint, placing him in a sitting position with the head between the knees is often effective in preventing an attack With syncope, the patient should be placed flat and the clothing loosened about the neck and any obstruction to breathing prevented Quick recovery without residual symptoms is the rule

Adams-Stokes Syndrome.—This condition is one of the important and serious causes of syncopal attacks Organic heart disease is usually present, although it may not be evident on physical examination Change of rhythm from a normal sinus rhythm or partial heart block to a complete heart block may be associated with cardiac arrest and the occurrence of faintness, giddiness, or unconscious attacks of varying severity (In some instances other mechanisms may be responsible for the attack and, unless one has an electrocardiogram during the seizure, it may be difficult to be certain of the exact pathologic physiology) A prefibrillary type of ventricular tachycardia with a very rapid ventricular rate may occur in some patients who have, as a basic rhythm, a complete heart block In others, short attacks of ventricular fibrillation with recovery may occur There may be no premonitory symptoms with these attacks The unconsciousness may persist for as long as one or two minutes and, if it is more than a few seconds, it is often associated with a generalized convulsion

In the *treatment* of this condition, it is important to know the exact cause of the attack by clinical observation, before and during the attack, and by electrocardiographic studies, whenever possible, during the spell An electrocardiogram between attacks may give valuable information In those cases with a basic normal rhythm or a partial A-V block, the attacks are usually the result of a change in rhythm with cardiac arrest prior to the beginning of a ventricular rhythm (A-V dissociation) The use of ephedrine, paradrine and similar drugs is indicated The newer synthetic atropine-like drugs may be tried in large doses and are sometimes effective in reducing attacks due to such mechanisms Digitalization as an aid to maintaining complete heart block is said to be effective at times In those patients in whom complete heart block is present and the attacks are due to prefibrillary ventricular tachycardia or ventricular fibrillation, the sympatheticomimetic drugs should, of course, be avoided The use of quinidine sulfate is indicated in these instances and should be given in doses of 0 4 gm (6 grains) or more every two to four hours The outlook in this type of patient is grave

Carotid Sinus Syncope.—This rather rare but interesting cause of syncope can usually be diagnosed, if suspected, by pressure over the carotid sinus area In many normal persons, especially those in the older age group, pressure on one or both carotid sinus areas produces a marked slowing of the heart Occasionally faintness or syncope may be produced In susceptible individuals, cardiac arrest may follow even slight pressure on this area In persons with a hypersensitive carotid

sinus, a syncopal attack may be produced by such a simple act as turning the head to one side

No special therapy is usually indicated for an attack of this type, but medications which increase vagal tone, such as digitalis, should be avoided in these individuals The use of atropine or the synthetic atropine-like drugs may be of value in preventing attacks, and sympatheticomimetic drugs such as ephedrine or paradrine may be utilized On rare occasions local conditions in the carotid sinus areas, such as tumors or enlarged glands, have been found to be the cause of such attacks and surgical therapy has proved effective in a few instances

PAROXYSMAL DYSPNEA

Under this heading may be included all types of paroxysmal shortness of breath from mild Cheyne-Stokes respirations to acute pulmonary edema The attacks may be mild and cause the patient only slight discomfort or difficulty in sleeping at night, or they may be severe enough to take the life of the patient They almost always represent a manifestation of severe cardiac disease The most common etiologic factor in this type of distress is hypertensive heart disease with left ventricular failure. Other causes are aortic insufficiency, especially of syphilitic etiology, active syphilitic aortitis without aortic insufficiency, coronary heart disease, and rheumatic heart disease In the latter instance, acute pulmonary edema is occasionally seen with advanced mitral stenosis, associated with the onset of a rapid tachycardia, or following severe physical effort At this time, extreme congestion of the lungs may result from the fact that the hypertrophied right ventricle pumps blood into the pulmonary bed in amounts which the stenotic mitral valve cannot pass through into the left ventricle Likewise the onset of a rapid tachycardia in the patient with hypertension or coronary disease may be accompanied by acute pulmonary congestion In these instances when the patient is hypertensive, the process may be accompanied by a marked drop in blood pressure, especially of the systolic pressure The patient may be unaware of the rapid action and dyspnea be the presenting symptoms

The *symptoms* of paroxysmal dyspnea depend on the severity of the condition When they are caused by Cheyne-Stokes breathing, the patient is not apt to be aware of the cause of his distress The most frequent complaint is inability to sleep and, if the patient is observed, it is seen that he is dozing or comfortable during the apneic phases and restless or agitated during the period of hyperpnea. Acute types of distress are seen with mild pulmonary edema and attacks of so-called "cardiac asthma " These spells are apt to occur at night and may awaken the patient from sleep He is quite distressed and sits on the edge of the bed and often gets out of the bed to a chair, or goes to a window to obtain more air Frequently, but not invariably, these conditions are accompanied by cough This may be severe and paroxysmal, but usually there is little sputum raised except during the most severe attacks

The patient may be conscious of a tightness in the chest associated with audible wheezes Auscultation of the chest in this stage is apt to reveal either numerous coarse moist rales over the bases of the lungs, or diffuse musical asthmatic type of rales associated with prolonged expiration, or difficulty in both inspiration and expiration The two findings may be associated in the same patient, or there occasionally may be a shift from one type to the other The patient is apt to have an ashen hue and perspire freely In hypertensive patients, the blood pressure may be elevated above the usual level during these attacks, although not necessarily so In the most severe attacks, which may develop very rapidly, the patient struggles for breath and audible moist rales are evident without a stethoscope Severe cough is usually present and there may be an abundant pink, frothy sputum.

Treatment of Paroxysmal Dyspnea Due to Cheyne-Stokes Breathing or to Mild Pulmonary Edema.—Correction of the underlying cardiac failure is usually sufficient to alleviate the condition Digitalization, diminution in the sodium intake, and the use of xanthine or mercurial diuretics may be sufficient to eliminate the trouble The use of a hypodermic of morphine sulfate, 16 mg ($\frac{1}{4}$ grain), is usually the best emergency therapy for both conditions Atropine with morphine is of doubtful value As a rule, it is not used by most physicians at the present time With Cheyne-Stokes breathing, morphine tends to increase the respiratory abnormality, but it may be counteracted by the use of aminophylline, given in doses of 0 5 gm ($7\frac{1}{2}$ grains) intramuscularly or often very satisfactorily by suppositories of this strength, inserted well into the rectum at bedtime Aminophylline 0 5 gm given slowly intravenously will usually give immediate relief in severe Cheyne-Stokes breathing

Treatment of the Severe Attack of Pulmonary Edema.—The patient with a severe attack of pulmonary edema presents an acute cardiac emergency which must be handled quickly and intelligently Again, the immediate use of a hypodermic of morphine, 16 mg ($\frac{1}{4}$ grain), is the first step Oxygen should be administered whenever possible, and the use of a pressure mask is of definite aid in improving this type of therapy One hundred per cent oxygen given by mask is the treatment of choice, although the use of a nasal catheter may be helpful The use of a mask may be interfered with by frequent coughing and the presence of large amounts of sputum, in the most severe cases

If the patient does not improve rapidly, the use of tourniquets on all extremities, in an effort to pool the blood in these regions, may be of definite value These should be applied high up on the arms and thighs and adjusted so as to allow the arterial pulse to come through, but to obstruct the venous return If these must be left on for a considerable time, one of the tourniquets can be loosened alternately for a short time every fifteen minutes Venesection, removing as much as 500 cc of blood rapidly, may occasionally be helpful

In a patient who is not receiving digitalis and who does not improve

within fifteen or twenty minutes, one should give a preparation of digitalis by the intravenous route if it is certain that the condition is due to cardiac failure and not secondary to acute myocardial infarction The glycosides of digitalis which act most quickly and are eliminated most rapidly are obviously the most desirable in this type of emergency The use of digoxin, 0 5 mg , or cedilanid, 0.8 mg given (undiluted) slowly intravenously, may be most helpful Preparations of purified solution of digitalis may be given in amounts of four to 6 U.S.P units (0 4 to 0 6 gm equivalent) under similar circumstances, but are probably less desirable than the former therapy Aminophylline, 0.25 to 0.50 gm , is a valuable drug and should also be given very slowly intravenously It may be mixed with the digitalis preparation without difficulty and the two drugs given simultaneously As a rule, therapy of this type will be effective in the average case In the more severe cases, especially those secondary to a recent myocardial infarct, the prognosis is grave

In occasional patients who show some improvement but still do not show satisfactory clearing of the lungs after one half hour to one hour, the use of an intravenous mercurial preparation may be helpful One cubic centimeter of one of the mercurial preparations suitable for intravenous use should be given slowly If the patient has previously taken such drugs and is known not to be sensitive to them, a 2 cc dose may be utilized

If the patient recovers from a severe attack of pulmonary edema as the result of acute cardiac failure, careful study of the etiologic factors concerned is indicated in anticipation of the patient's future management The use of low sodium or a salt-free diet is indicated in addition to continuous digitalis therapy and mercurial or xanthine diuretics may need to be utilized Limitation of the patient's activity is of course indicated If the etiologic factor of the paroxysmal dyspnea is syphilis, careful antiluetic therapy is indicated In these instances, where such attacks are the manifestation of early aortic insufficiency, or severe aortitis, this type of therapy may be instrumental in preventing a rapid progression of the disease There is considerable evidence accumulating that intensive penicillin therapy may be relatively safe in this type of case

ACUTE HEART FAILURE

Heart failure is occasionally a medical emergency Usually the condition develops gradually and treatment is started before the condition is serious However, at times because of lack of medical care or for other extenuating circumstances, the patient may not been seen until serious failure has developed and his condition is critical Shock or peripheral circulatory failure must be differentiated from acute heart failure The salient features of the two are well known and the differential points will not be discussed here Suffice to say that the two may occur together occasionally with acute myocardial infarction As a rule, both

right and left ventricular failure occur together, although one or the other may predominate and rarely a condition close to isolated failure is seen

There are many precipitating factors which may precede the development of acute cardiac failure These conditions should be sought for and recognized, especially in those patients who have not had previous cardiac disease Among these are acute infectious processes in the older age group and in patients with rheumatic heart disease, hypertension, acute coronary thrombosis, and the development of an ectopic rhythm as auricular fibrillation or paroxysmal tachycardia. The diagnosis of acute cardiac failure is seldom in doubt, but in appraising the situation, it is important to determine what etiologic factors are present, and what precipitating factors may be operative The treatment may be modified by the underlying cardiac condition This is especially true in the case of acute coronary thrombosis with myocardial infarction The following case report illustrates a number of important points in the therapy of acute heart failure

Case Report —G F , a white man, aged 60, was admitted to the Pennsylvania Hospital at 4 00 A.M , December 26, 1948, because of severe dyspnea His acute symptoms had begun about four hours before, while sitting quietly listening to the radio Increasing exertional dyspnea had been present for a period of about six months and had been severe enough to cause him to seek medical advice about nine weeks prior to admission The dyspnea had increased rather markedly during the last week There was no history of cough, chest pain, or increasing edema Systemic review and past medical history was essentially negative, except for obesity of many years' duration and rather prolonged intermittent treatment for latent syphilis

Physical examination on admission to the hospital revealed an obese, cyanotic, dyspneic and apprehensive white male, who appeared acutely ill There were coarse, moist rales heard throughout all lung fields The heart showed slight enlargement to the left, though examination was difficult because of obesity and emphysema The rhythm was irregular with a rate of about 160, and the heart sounds were distant No murmurs were heard The abdomen was very obese No enlargement of the liver or spleen was found The lower extremities showed slight pitting edema The blood pressure was 150/108 and there was considerable pulse deficit

Emergency treatment consisted of morphine sulfate 10 mg ($\frac{1}{6}$ grain) subcutaneously and continuous oxygen Four U S P units of digalen and 0 25 gm ($3\frac{3}{4}$ grains) of aminophylline were given slowly intravenously The patient improved rapidly and 0 4 gm (6 grains) of digitalis leaves were given by mouth. Within a few hours he was much improved, but a heart rate of 156 per minute with a regular rhythm was noted the day after admission It was found that pressure over the right carotid sinus area caused the heart rate to slow to about 80 to 90 per minute, during the time of pressure The rate returned to 156 per minute with release of the pressure and the rhythm was again regular A clinical diagnosis of auricular flutter was confirmed by the electrocardiogram (see Fig 259, *A*) Only a few moist rales were present at the extreme bases of the lungs after forty-eight hours of therapy

With the patient nearly free from cardiac failure, consideration was given to treatment of the auricular flutter and the obesity He was placed on a low calorie,

low salt diet, and digitalis leaves were given in doses of 0 4 gm (6 grains) on each of the next three days An increase in the degree of A-V block was noted on December 29 (Fig. 259, *B*) On the following day 0 6 gm (9 grains) of digitalis was given On January 1, 1949, the rhythm was found to be perfectly regular and it was suspected the patient had reverted to normal sinus rhythm No nausea had occurred up to this point, despite the rather large dosage of digitalis He was placed on a maintenance dose of digitoxin 0.2 mg for the next three days An electrocardiogram on January 3 (Fig 259, *C*) showed the rhythm to

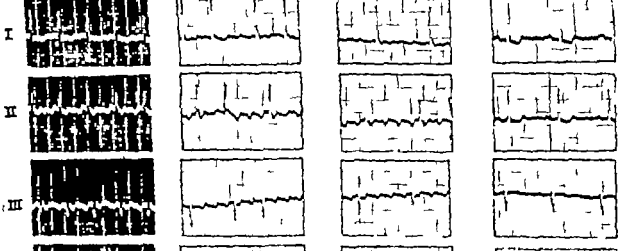

Fig 259 —A white man, aged 60, with obesity and arteriosclerotic heart disease, experienced a gradual loss of cardiac reserve over a six month period, with emergency admission to the hospital for acute pulmonary edema on December 26, 1948 *A*, taken after a total of 0.8 gm (12 grains) of digitalis shows auricular flutter to be present with an auricular rate of 280, and a ventricular rate of 140 per minute *B* was obtained after a total dose of 1 6 gm (24 grains) of digitalis and shows that auricular flutter persists with a variable A V block, (2 1, 3 1, and 4 1) The auricular rate is 320 per minute *C* demonstrates a stable 4 1 A V block obtained after a total digitalis dosage of 3 gm (45 grains) The auricular and ventricular rates are 296 and 74, respectively Normal sinus rhythm was resumed on January 7, 1949 after a total of 4 6 gm (69 grains) of digitalis in eleven days *D* shows the electrocardiogram on this date Left axis deviation "digitalis effect" on the RST segments and large amplitude of the QRS complexes in the precordial lead, are evident (Other precordial leads were taken but showed no significant changes and are not included in order to save space)

be auricular flutter with 4 1 A V block, rather than normal sinus rhythm The patient was becoming ambulatory at this time and it was noted that the heart rate would increase rapidly with slight effort This was both irregular and regular with a heart rate as high as 160 for short intervals The digitalis dosage was again increased to 0 4 gm. (6 grains) daily on January 4, 5, and 6 On January 7 the patient complained of rather severe nausea for the first time The heart rate was found to be stable and regular at a rate of 80 per minute and the blood pressure was 134/80 Electrocardiogram showed normal sinus rhythm to be present (Fig 259, *D*) Digitalis was stopped and the patient continued to improve though nausea persisted for several days.

The patient was placed on a maintenance dose of digitalis leaves, 0 1 gm (1½ grains) daily, and discharged much improved on January 15, 1949 An electrocardiogram taken on that date showed normal sinus rhythm to be still present The patient continued to lose weight and six months later was symptom-free and back at his usual job as a commercial artist The maintenance dose of digitalis was continued

Comment—This patient illustrates the rapid response of acute pulmonary edema due to left ventricular failure to the usual therapy of morphine, oxygen and supportive medication The etiologic factors concerned were probably a combination of prolonged mild hypertension, coronary sclerosis and obesity It seems likely that auricular flutter may have been present for some time prior to the actual development of failure, as the patient had been given Lugol's solution for a "rapid heart rate" a short time before Digitalis therapy, given orally in divided doses over several days, as was done in this patient, is usually successful in terminating auricular flutter As a rule, a much larger daily and total dosage is needed than would be utilized in digitalizing the average patient An attempt is made to convert the flutter to auricular fibrillation If and when this occurs, the digitalis is stopped and the rhythm will often revert to normal In this patient no actual period of auricular fibrillation was observed though it probably occurred

Careful observation is essential when such large doses of digitalis are used A toxic effect to be watched for is ventricular ectopic beats Frequent electrocardiograms are helpful and often a necessity The digitalis must often be pushed to the point of nausea or even vomiting to break the rhythm If digitalis therapy is not successful, quinidine therapy, as described later in this chapter, should be tried

Emergency Treatment.—Occasionally patients are seen with severe cardiac failure in whom prompt therapeutic measures are essential to save the life of the patient In this type of patient, the heart rate may be rapid or slow and the rhythm regular or irregular More often than not the patient is suffering from auricular fibrillation with a rapid ventricular rate, and the underlying etiologic heart disease is either rheumatic heart disease with mitral stenosis or arteriosclerotic heart disease, with or without hypertension

The treatment of a patient of this type who has received no previous digitalis preparation is primarily one of rapid digitalization with supportive and symptomatic therapy Unless the patient is semicomatose, it is usually wise to give a hypodermic of morphine sulfate, 16 mg (¼ grain), in the upper extremity to allay apprehension and to reduce the cough and dyspnea The use of 100 per cent oxygen by face mask is desirable whenever possible and when the patient will tolerate this type of therapy The patient is usually orthopneic and there is no objection to his sitting in a chair This position may actually be desirable in those patients with marked edema of the lower part of the body

Digitalis glycoside preparations are the backbone of therapy of this type, and the use of the drug *intravenously* is the method of choice

Absorption of even the most rapid acting of the glycosides is not satisfactory by the *oral* route in patients with this condition The congestion of the organs of the gastrointestinal tract make it obvious that any such therapy will not be rapidly effective The use of these preparations subcutaneously or intramuscularly has been practiced in the past, but there is much evidence that the absorption of the drug is delayed in these patients and this route is not satisfactory The more rapid acting digitalis glycosides should be utilized in these cases.

In patients who have received no previous digitalis for a period of at least two weeks, it is safe to use digoxin, 0 5 mg , or cedilanid, 0.8 mg , as the first does These drugs should be given slowly and undiluted If one of the purified solutions of digitalis is used, the initial dose should be 0 4 gm equivalent, (usually 4 cc or 8 cc of the preparation for intravenous use) A second injection of one-half of the original dose may be given intravenously in thirty to sixty minutes if the patient does not show definite improvement Preparations of Strophanthus given parenterally are preferred by some

It should be remembered that patients who are developing congestive failure often take large doses of digitalis to break the cycle and one should not hesitate to push the drug if he is certain of the diagnosis and if it is done with careful observation of the patient In patients with rapid auricular fibrillation, the heart rate is the important point of observation (the pulse deficit in these cases is related to the ventricular rate and, as this rate drops, the pulse deficit diminishes There may be a reduction of 30 to 60 beats or more per minute in the first thirty minutes in those patients with rapid ventricular rates)

In patients who have been given unknown amounts of digitalis, it is wise to reduce the above doses somewhat However, in patients with auricular fibrillation with a rapid ventricular rate it can usually be assumed that inadequate doses of digitalis have been used As the patient shows definite improvement, digitalis by mouth should be instituted

Other drugs which may be of value in patients who are in extreme cardiac failure are intravenous aminophylline and mercurial diuretics Again these drugs should be used intravenously, and aminophylline, 0.25 gm (3¾ grains) or 0.5 gm (7½ grains), may be combined with 1 cc of a mercurial diuretic and the two given together very slowly No food is necessary or desirable for several hours There is no objection to sips of water by mouth and, as the patient improves, small amounts of liquid or soft foods may be given The use of the Karell diet (200 cc of milk four times daily) is very satisfactory for a few days in patients of this type

Acute severe heart failure is less frequent with normal rhythm and slower heart rates than with rapid auricular fibrillation It occurs occasionally, however, and the therapy is not different than that outlined for auricular fibrillation The same is true of patients who are suffering from persistent paroxysmal tachycardia or auricular flutter The exception is cardiac failure with ventricular tachycardia This condition prec-

tically always occurs in patients with severe cardiac disease and very often following myocardial infarction Not infrequently the patients have been receiving digitalis With the sudden appearance of tachycardia in such patients, an electrocardiogram is essential to confirm the suspicion of a ventricular origin for the ectopic rhythm This condition is frequently a precursor of ventricular fibrillation and the prognosis should be guarded

THE PAROXYSMAL TACHYCARDIAS

There are a number of types of paroxysmal rapid heart action, any of which may produce clinical symptoms and present a cardiac emergency This is especially true if the patient suffers from organic heart disease At the onset of very rapid heart action, faintness or syncope may occur The common types of paroxysmal tachycardia are (1) supraventricular tachycardia, usually auricular, (2) auricular flutter and (3) auricular fibrillation

Supraventricular Tachycardia.—The most frequent type of paroxysmal tachycardia, and the one usually referred to when this term is used, is a supraventricular tachycardia, with the focus of origin in the auricle or high up in the A-V node It is characterized by a sudden onset and usually, but not invariably, by a sudden cessation The attacks vary in duration from a few minutes to a few hours, and rarely may last for several days They frequently occur in patients without evidence of organic heart disease In patients with organic disease, they are more serious and the signs of cardiac insufficiency may develop fairly rapidly The heart rate is usually above 160 per minute and not infrequently is more than 200 per minute The rhythm is absolutely regular and there is no pulse deficit The pulse is usually small due to a drop in blood pressure and a small pulse pressure, consequent to insufficient time for filling of the ventricles

The *diagnosis* of paroxysmal tachycardia can usually be made from the history and observation of the patient

Treatment —Sustained pressure over the carotid sinus area may terminate the attack abruptly This is more often successful when applied to the right side The patient should be lying flat with one pillow under the neck and the head tilted slightly backward (The carotid artery is located below the sternocleidomastoid muscle with the first three fingers, and steady pressure is applied mesiad and cephalad, for a period of several seconds Auscultation of the heart should be carried out coincident with this procedure Occasionally the left carotid sinus area will be successful when the right is not, but pressure should not be made on both sides at the same time Retching or vomiting may terminate an attack Persons who have frequent attacks may learn methods by which they can themselves arrest the attack Sedatives, and an ice bag to the precordium are occasionally of value The patient should be kept in the recumbent position

If the attack persists more than a few hours, quinidine therapy in

doses of 0.33 to 0 4 gm (5 to 6 grains) every hour for three or four doses should be tried It is well to give an initial dose of 0 2 gm (3 grains) to determine possible sensitivity to this drug In patients with severe organic disease it may be desirable to terminate the attack as soon as possible If the simple methods are not effective, rapid digitalization in those patients who have not been receiving the drug is a valuable procedure The use of a rapidly acting, quickly eliminated glycoside is desirable in such cases Digoxin, 0.5 mg , or cedilanid, 0.8 mg , given slowly intravenously is often successful If the attack does not stop after a few minutes, carotid pressure should be tried again The dose may be repeated in an hour if the original dose is not successful In most patients, the attacks will be terminated by such a procedure

Paroxysmal Auricular Flutter —This condition is usually seen in patients with organic heart disease It is characterized by a rapid and regular heart rate from 120 to 180 per minute It is not often that a heart rate above 160 per minute is present, but not infrequently rates as low as 120 occur In these instances, the ectopic rhythm is apt to be overlooked because of the relatively slow rate There is usually a 2 1 A-V heart block so that a ventricular rate of 120 will be present with an auricular rate of 240 Auricular waves may be evident in the venous pulse, but these are easily overlooked and may not be visible In contradistinction to paroxysmal auricular tachycardia where carotid sinus pressure either produces no effect or causes abrupt cessation of the attack, pressure of this type in patients with auricular flutter is apt to *slow* the ventricular rate *while* the pressure is applied This is the result of an increase in the A-V heart block so that a 3 1, 4 1, or even greater heart block is produced with a consequent slowing of the ventricular rate As the carotid pressure is released, a return to the former rate occurs Although this clinical test is not diagnostic, it is very suggestive of the presence of auricular flutter

The *diagnosis* is usually obvious in the electrocardiogram although at times, in the leads commonly taken, the auricular flutter waves are not easily seen In such instances, a precordial lead from the C_4 position (fourth right intercostal space adjacent to the sternum) will usually demonstrate the flutter waves very well

Treatment —The most frequently successful and safest treatment is digitalization The case report under the heading of "Acute Heart Failure" illustrates this type of therapy If full doses of digitalis are not successful or if toxic effects of digitalis contraindicate its further use, quinidine therapy should be tried This drug is occasionally successful when digitalis fails and in the absence of heart failure it can be used safely in fairly large doses after digitalis therapy After a test dose of quinidine sulphate of 0.2 gm (3 grains), the drug should be tried for a day in doses of 0 4 gm (6 grains) every four hours This should be increased to 0 4 gm every three hours on the second day If such dosage is not successful and no toxic effects have been noted, larger doses over short periods of time should be tried A single dose of 0 6 gm (9 grains)

followed by a similar dose in one or two hours may be successful On the following day, three doses of 0 6 gm each, one or two hours apart, should be tried if smaller doses have not accomplished their purpose Careful clinical observation of the patient during intensive quinidine therapy is imperative and electrocardiographic control is nearly a necessity

Auricular Fibrillation.—Attacks of paroxysmal auricular fibrillation are seen in patients with and without heart disease In the latter instance, the attacks are a manifestation of cardiac irritability and are apt to be precipitated by severe exertion, fatigue and alcoholic or smoking excesses The attacks are apt to last from a few hours to a few days and usually terminate spontaneously Usually the ventricular rate is very rapid in this type of patient because of the normal conduction system Because of this, there is a drop in blood pressure as well as considerable *pulse deficit* and symptoms of circulatory insufficiency as vertigo, weakness or syncope may occur This is especially true at the onset of the attack In patients with organic heart disease, paroxysmal attacks are apt to occur in those with slight rather than severe disease They are seen especially in mitral stenosis, hyperthyroidism and arteriosclerotic heart disease There is apt to be a precipitating factor such as injury, infection, undue exertion, or even such minor conditions as abdominal distension Attacks are not infrequent postoperatively or after an attack of acute myocardial infarction, in the older age group of patients After a day or so, the attack is apt to subside spontaneously if the patient's general condition improves, or if the precipitating factor is removed

The *diagnosis* of paroxysmal auricular fibrillation is easily confirmed by clinical examination The rapid heart rate with a totally irregular rhythm and a pulse deficit leave no doubt as to the mechanism (It is essential to listen to the heart and take the pulse simultaneously The more rapid the rate, the greater the pulse deficit The latter depends on the ventricular filling and, because the auricles are not contracting, the ventricular filling is less satisfactory than with an equivalent tachycardia from another cause)

Treatment—In the treatment of paroxysmal auricular fibrillation, the patient should be kept quiet even though there is no evidence of organic heart disease If the patient has had previous attacks, he is usually not greatly alarmed, however, there may be marked palpitation and even precordial or substernal distress with very rapid rates associated with a marked drop in blood pressure Mild sedation or morphine hypodermically, and an ice bag to the precordium are helpful as immediate measures As some of these patients are very responsive to quinidine, one dose of 0 2 gm (3 grains) may be given by mouth and repeated in one hour In patients with obvious organic heart disease, or in any patient with evidence of beginning cardiac failure, it is usually not wise to begin with quinidine therapy If the attack does not stop spontaneously in a few hours (which it often does, even in pa-

tients with organic disease), the patient should be rapidly digitalized by the oral route An initial dose of 0 6 mg of digitoxin or 0 6 gm of digitalis leaves should be given, followed by 0.2 gm of digitoxin or 0.2 gm of digitalis leaves every four hours until a total dose of approximately 1.2 mg of digitoxin or 1.2 gm of digitalis leaves is given If there has been no marked slowing of the heart rate, this dose schedule should be continued for another twenty-four hours and the patient watched carefully

Reversion to normal sinus rhythm is rather frequent with this type of therapy If it does not occur, small doses of quinidine are then apt to be effective An initial dose of 0.2 gm (3 grains) may be given, followed by doses of 0 4 gm (6 grains) at the end of two hours and four hours This dosage should be repeated in twenty-four hours if it has not been effective Larger doses may be safely utilized in patients with minimal cardiac disease

There is some difference of opinion regarding the treatment of patients with *myocardial infarction* who develop auricular fibrillation As mentioned, this is apt to occur in the older age group and is frequently a paroxysmal affair If there are no signs of cardiac insufficiency, it is probably safe to give 0.2 gm (3 grains) of quinidine every four hours for one or two days. Reversion to normal rhythm is apt to occur in this period of time if the patient shows improvement in his general condition This disturbance of rhythm is likely to be seen early in the attack, and all of the usual types of therapy should be utilized With early signs of cardiac failure, a low sodium diet with parenteral mercurial diuretics should be tried before resorting to digitalization With continuation of the auricular fibrillation and progression of the signs of failure, digitalization should be carried out in order to slow the ventricular rate and decrease the cardiac insufficiency If reversion to normal sinus rhythm does not follow restoration of compensation, small doses of quinidine are then apt to be effective Some authors advocate the use of quinidine, 0.2 gm (3 grains) every four hours, concomitantly with digitalis, in this type of patient

Occasionally an attack of auricular fibrillation of the paroxysmal type may persist and become chronic This is usually seen in patients with some organic disease If the degree of heart trouble is not great, it is usually wise to attempt to restore the rhythm to normal In these instances, the patient should be digitalized and the ventricular rate well controlled Then, intensive quinidine therapy should be given as described under "Auricular Flutter"

PULMONARY EMBOLISM

The present awareness of the medical profession to thromboembolic disease has made the diagnosis of pulmonary embolism a much more common occurrence than it was a few years ago In the years of 1911 and 1915, the diagnosis of venous *thrombosis* and/or pulmonary embolism was made in ninety four patients at the Pennsylvania Hospital

In the years 1947 and 1948, the diagnosis was made 196 times in approximately the same number of hospital admissions It seems likely that a higher degree of suspicion and more accurate diagnosis is responsible for the difference in the number of patients during the latter period, rather than any significant difference in the number of cases With the reduction in surgical mortality resulting from improved surgical technics and anesthesia, death from pulmonary embolism in postoperative patients is assuming increasing importance The more clinical recognition of this condition has shown that many common medical patients have their illness complicated by pulmonary embolism In patients with acute myocardial infarction, the mortality from pulmonary embolism is quite appreciable Careful inspection of the lower extremities in patients with chronic disease and in postoperative patients may reveal tenderness on pressure over the calf muscles or a positive Homans' sign, which are suggestive of phlebothrombosis Acute thrombophlebitis may also be a precursor of pulmonary embolism Frequently there are no symptoms or signs to suggest that pulmonary embolism is imminent

The *symptoms* of pulmonary embolism depend on the size of the embolus, the general condition of the patient, and particularly the condition of the lungs Pulmonary *embolism* is not synonymous with pulmonary *infarction* Whether or not an infarct forms following embolism of the lungs depends on a number of factors It was once thought that it was nearly impossible to infarct a normal lung, but it is now known that this is not correct In chronic passive congestion of the lungs as is seen in heart disease, especially with mitral stenosis, small pulmonary emboli may produce large hemorrhagic infarcts In other patients, large emboli may lodge in one of the main pulmonary arteries without the production of a demonstrable infarct by clinical examination or x-ray In some of these patients, death may occur too rapidly for an infarct to form, but in many who recover, no evidence of infarction is found

Massive pulmonary embolism is apt to be of sudden onset without premonitory signs or symptoms The patient is taken with extreme dyspnea and distress in the chest, usually substernal, following some slight exertion or, perhaps, straining on the bed pan Not infrequently it may occur when the patient is getting up and about for the first time following a surgical operation The victim appears more or less shocked with a rapid, thready pulse, low pulse pressure, perspiration, ashen-gray hue, and a subnormal temperature The appearance of the patient and the symptoms may be very suggestive of acute coronary occlusion with myocardial infarction In the fatal cases, death is not instantaneous, but the patient is apt to live for a few minutes or for a period of one or two hours If the patient survives a few hours, he is apt to recover unless further emboli occur

With smaller pulmonary emboli, the manifestations may be less striking and less clearcut In these patients, the diagnosis is apt to be missed unless the clinician is alert Pulmonary embolism with infarction is

frequently manifested by pleuritic pain, most often present over one of the lower lobe areas, or occurring in the upper abdomen or shoulder Hemoptysis is occasionally the only manifestation of pulmonary embolism The sputum, in these instances, is usually dark red and mucoid Shock, in such cases, is usually not present and the nature of the pleurisy or hemoptysis is easily overlooked

In the *diagnosis* of pulmonary embolism, a healthy suspicion is of greater value than most of the laboratory procedures The recognition of the predisposing factors as well as the nature and manifestations of pulmonary embolism is essential for every physician if the lives of these patients are to be saved Acute myocardial infarction is the condition which must frequently be differentiated from pulmonary embolism As the therapy for these two conditions is somewhat similar, it is not always essential that they be differentiated during the first few hours The occurrence of *blood spitting* or of *acute pleurisy* in patients who are a few days postoperative is most suggestive of pulmonary embolism A careful search for the source of emboli in the lower extremities is important, but it should be recognized that such emboli frequently come from the pelvic veins or from the operative site In view of the extreme importance of therapy in preventing subsequent pulmonary emboli, it is often desirable to make a presumptive diagnosis of pulmonary embolism and start treatment

The diagnostic laboratory aids which may be helpful in some patients are the x ray and the electrocardiogram Some changes are present in the x-ray in a fairly high percentage of all cases if careful studies are done, but these changes are not necessarily diagnostic of pulmonary embolism or infarction Bedside films are seldom satisfactory, and it is usually unwise to move patients with pulmonary emboli for a few days after embolization Abnormal electrocardiographic changes are demonstrable in a fairly high percentage of the patients if records are taken as soon as possible after the embolization, and if repeated records are taken The changes may be fairly characteristic of pulmonary embolism (Fig 260), or there may be acute changes suggesting coronary insufficiency which return to normal fairly rapidly, as the patient recovers

The *prognosis* of pulmonary embolism depends on the size of the embolus, the condition of the lungs, and the general condition of the patient at the time of embolization As many as 40 per cent of patients with very large pulmonary emboli succumb within a few minutes to a few hours after the initial attack Of those who survive, about 25 per cent will die from a later embolus or emboli if proper therapeutic measures are not carried out

Treatment—In the emergency treatment of acute pulmonary embolism, the important considerations are relief of dyspnea and apprehension, and the combating of anoxia and shock If the patient can survive the first few hours, recovery is apt to occur As many of the patients who develop this condition are already hospitalized, medical and nursing care are frequently available at once A hypodermic of 10

to 16 mg ($\frac{1}{6}$ to $\frac{1}{4}$ grain) of morphine sulfate may help in allaying distress and apprehension

There is some disagreement among authorities regarding medication to combat pulmonary artery spasm It is possible that papaverine hydro-

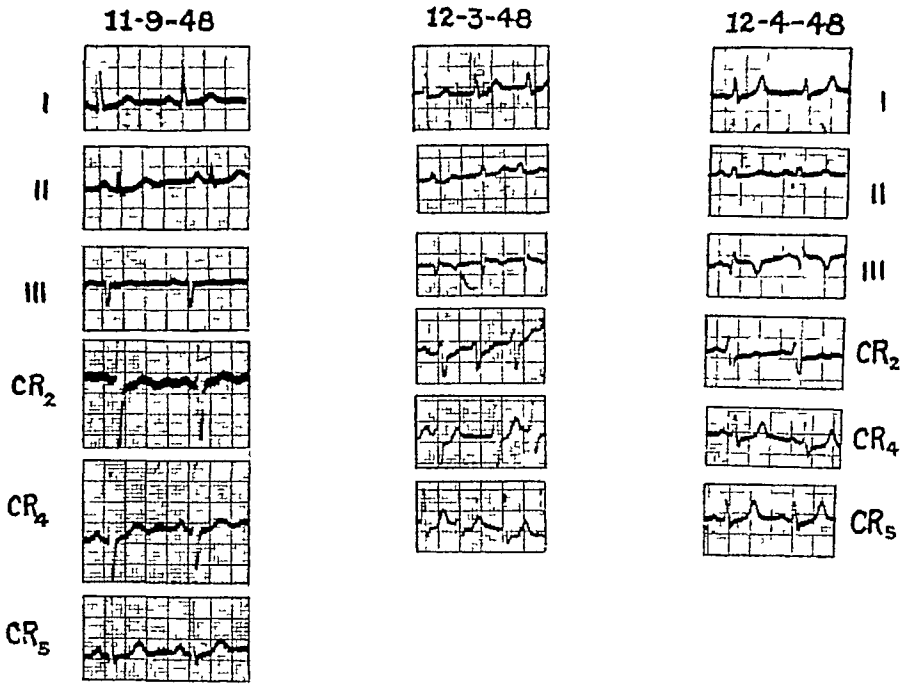

Fig 260 —F W , a 62 year old woman, was hospitalized on November 1, 1948 for intestinal obstruction Operation on November 11 revealed widespread metastases to the peritoneum from cancer of the uterus A palliative cecostomy was done On December the third, the patient suddenly became dyspnoeic and went into profound shock The pulse was small, rapid and irregular, and the blood pressure was approximately 66/56 She gradually lapsed into coma and died in about twenty-four hours Postmortem examination revealed several large pulmonary emboli composed of masses of tumor cells and blood clots The heart showed no significant abnormalities

The preoperative electrocardiogram of November 9, 1948 shows only a left axis deviation The record of December 3, 1948, taken about three hours after the onset of the acute symptoms, shows auricular fibrillation, RS-T_1 and RS-T_2 segments depressed, a deep Q_3 wave with elevated RS-T segment in this lead, and depressed RS-T segments in the precordial leads The record of December 4, 1948, taken fifteen hours later, shows a return to normal sinus rhythm but persistence of the S_1-Q_3 pattern, and the RS-T segment changes

chloride, 65 mg (1 grain), and atropine sulfate, 0 9 mg ($\frac{1}{75}$ grain), given intravenously may be of value in this regard

Oxygen (100 per cent) by mask should be started at once and if the patient is holding his own or showing some improvement after one or two hours, consideration should be given to starting anticoagulant therapy in those patients in which the diagnosis seems established Fifty milligrams of heparin, undiluted, should be given intravenously,

and further therapy with heparin and Dicumarol be carried out as described elsewhere in this symposium In those patients in whom coronary thrombosis and pulmonary embolism must be differentiated, electrocardiograms, as previously mentioned, may yield valuable diagnostic information Electrocardiograms may be obtained without disturbing the patient or his treatment Since anticoagulant therapy has also proved of value in the treatment of myocardial infarction, it is not necessary to delay this type of therapy if the probable diagnosis rests between these two conditions

DIABETIC COMA

GARFIELD G DUNCAN, M D, F A C P,* LAWRENCE S CAREY, M.D,† AND MANNING T HUDSON, M D ‡

There is no greater emergency in the field of internal medicine than diabetic coma Yet, this dangerous complication is preventable It will not develop while the diabetes is under good control It is recognizable in its early phases at which time its correction is a simple matter It is amenable to treatment even when it has escaped detection and remedial measures during its development Progressive improvement in therapy behind these truths explains why the mortality from diabetic coma has been reduced dramatically The fact that there have been no deaths from diabetic coma at the Pennsylvania Hospital in over two and one-half years is a stimulus to continue, without relaxation, to improve the instruction of diabetic patients, to identify ketosis in its incipiency and to improve the therapy for diabetic coma Diabetic coma is still a medical emergency of a major degree and recovery from it depends upon its early recognition, an understanding of the mechanisms at work, and appropriate measures directed toward reversing the processes which, if not corrected, lead to a fatal termination

NATURE OF DIABETIC COMA AND ITS DIAGNOSIS

Diabetic ketosis, progressing until the patient is in a state of coma, occurs when the utilization of carbohydrate is reduced to a degree which causes an increase of great magnitude in the metabolism of fat As a result, acetone bodies (acetone, diacetic acid and beta hydroxybutyric acid) are produced at a rate which exceeds the ability of the body to complete their oxidation and the excess, in the early stages, is excreted in the urine As this process progresses 1 plus reactions for acetone in the urine are replaced by 2 plus, 3 plus, and finally 4 plus reactions The kidneys, and to a minor extent the lungs, can carry off, for variable periods, the excess acetone bodies from the blood but, barring relief, finally acetone production exceeds the functional capacity of the excretory mechanisms and acetone bodies accumulate in the blood At first, this stage is detectable by the appearance of traces of acetone in the blood plasma but, barring correction, 2 plus, 3 plus, and finally 4 plus qualitative reactions for plasma acetone are observed It is not until 4 plus reactions for acetone in the urine are observed for variable periods that amounts of acetone increase in the plasma to a sufficient

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concentration to be detected by the usual tests employed Hence a 3 or 4 plus reaction for acetone in the plasma indicates a much more advanced degree of ketosis than do similar reactions obtained on examination of the urine

The diabetic patient having 4 plus reactions for glycosuria and acetonuria, and a 4 plus reaction for plasma acetone fulfills the chemical criteria necessary to make the diagnosis of diabetic coma The diagnosis can be made at the bedside Urine for testing is obtained by catheter if necessary and 10 cc of oxalated blood allowed to stand for a few minutes will provide plasma or serum of which only two drops are needed in the tests for acetone *

Excessive ketone production provides the clue to the diagnosis and the early detection of this clue is of extraordinary importance The simplicity of the tests for plasma acetone puts a precise and valuable diagnostic measure in the hands of every physician The diagnosis can be established without elaborate equipment or technical assistance and —of most importance—therapy can be started at once It is practicable then, even in remote places, to give a patient in diabetic coma the opportunities of recovery closely approaching those enjoyed by patients in large cities with nearby hospital facilities In case of the latter group their chances of recovery from diabetic coma are also greatly enhanced if the diagnosis is made in the home and not delayed until the patient is admitted to the hospital We know of a patient in whose case the diagnosis was made, 100 units of insulin and 8 ounces of well salted broth were given within thirty minutes of the time the physician saw the patient This illustrates what can be the next great advance in the management of diabetic coma—immediate diagnosis with insulin and sodium chloride administration begun in all cases preliminary to moving the patient to the hospital

Prior to and in the early stages of ketosis important disturbances in the patients' fluid and electrolyte balances have been taking place,

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* 1 *Rothera-Wishart Test for Acetone in the Plasma* Two drops of plasma, or serum, are placed in a Wassermann tube and supersaturated with ammonium sulfate crystals and shaken Two drops of approximately 5 per cent sodium nitroprusside solution are added and shaken Two drops of ammonia water are added and shaken Allow to stand for three minutes

Interpretation	Permanganate color	trace of plasma acetone
	Light blue	moderate
	Deep blue or almost black	heavy reaction for plasma acetone

2 *Acetone Test* (Denco) This simple and accurate test for acetone is executed by depositing on a dry white paper sufficient of the Acetone Test (Denco) reagent—containing sodium bicarbonate, ammonium sulfate and sodium nitroprusside in anhydrous form—to cover the size of a little fingernail and by moistening this entire amount of powder with two or three drops of the plasma to be tested In the presence of acetone a shade of purple will develop within thirty seconds, a trace of acetone yields a light lavender color and with increasing amounts the color will be darker, a dark blue indicating a 4 plus reaction In the absence of acetone a grayish-yellow color is the result

notably the increased hyperglycemia with its diuretic effect, the loss in the urine of large quantities of sugar and of base, especially sodium and, to a smaller degree, but nevertheless of great importance, potassium All have a bearing on the clinical state of the patient and on the therapy necessary These later considerations account for the *intense dehydration, hemoconcentration, increased specific gravity of the whole blood, low and at times imperceptible blood pressure, vascular collapse* with evidences of the resulting *renal incompetence* as indicated in the gravely ill patient by *oliguria* with *albumin* and *granular casts*, or in some instances by *anuria* with the development of the *uremic state*, if correction is delayed If the shocklike state prevails for many hours, changes in the renal tubules characteristic of a lower nephron nephrosis may occur In such cases the *excessive* administration of fluids is fraught with great danger

Second only in importance to an early diagnosis and insulin therapy are the halting and correction of these secondary and dangerous processes Administration of salty broth orally as soon as the diagnosis is made will often turn the tide favorably and in some cases will be life saving Most medical writings deal almost exclusively with diagnosis and treatment of coma in hospitalized patients This communication stresses also what can be done in the field so to speak, or, as it were, at the front line before evacuating the patient to the hospital

PRECIPITATING CAUSES OF DIABETIC COMA

Any factor or factors which increase total tissue metabolism with one exception—physical exercise—tend to intensify the diabetes and as a result increase the need for insulin Illustrations of this effect are observed in cases of thyrotoxicosis, pregnancy, febrile disturbances and gain in body weight A diagrammatic illustration of the reduction in the effectiveness of insulin during acute complications is presented in Figure 261

The unfavorable influence of increasing total metabolism alone or when combined with other features which predispose to and cause diabetic coma may precipitate a clinical emergency with great rapidity The pregnant and the thyrotoxic diabetic patients who develop acute infections illustrate this group, as do the neglected obese diabetic patients who acquire staphylococcic skin infections, notably carbuncles Also, the patient who disregards—by ignorance or indifference—dietary restrictions and overeats with the result that the diabetes is out of control, is predisposed to develop ketosis when a precipitating factor makes its appearance The latter patient is like the chauffeur who boasts of how closely he can drive to the edge of a high cliff He or she is a candidate for a rapidly developing ketosis in the event of infections, even of a minor nature, gastrointestinal disturbances (vomiting or diarrhea), surgical complications and the omission of insulin It is remarkable how frequently the diabetic patient who, because of anorexia, during an

acute complication omits insulin This may be done with or without the advice of a physician In such cases the anorexia is frequently due to ketosis in its early stages and all that remains to speed the quickest possible development of coma is the withdrawal of insulin therapy The anorexic diabetic patient is a potential emergency at all times but when the anorexia is associated with some other disorder be it an upper respiratory tract infection, gastrointestinal upset or one of the possible multitude of complications, the emergency exists and careful clinical evaluation and therapy are necessary if needless risk is to be avoided. Such patients *who exhibit strongly positive reactions for glycosuria* and *acetonuria* and whose *plasmas give a 3 plus or 2 plus reaction for acetone are in the pre-coma state*

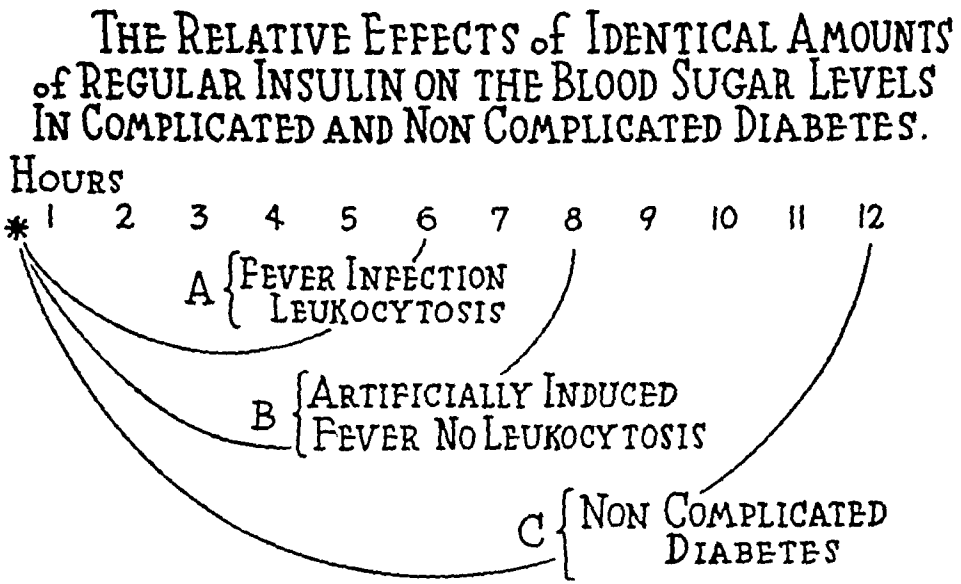

Fig 261 —The differences in the blood sugar lowering effect and the duration of the effectiveness of identical doses of regular insulin under normal and abnormal circumstances are diagrammatically presented

The anorexia of the diabetic patient suffering from an acute clinical condition is intensified by nausea and with the onset of vomiting and its unfavorable influence on the fluid balance and chloride depletion the dehydration and vascular collapse in these patients are quickened

Sodium chloride administered as salty broth in the anorexia phase may halt and will certainly postpone the downward progress We have repeatedly observed that this simple measure has alleviated nausea and vomiting often ceases when salty broth is ingested. Failing and early diagnosis or early treatment, or both, the ketosis gains headway slowly —several days to weeks—in the neglected diabetic without acute complications but the ketosis develops very rapidly—a matter of hours—in the presence of acute infection and toxemia

PREVENTION

Diabetic coma is preventable but to achieve this goal patients must be trained thoroughly concerning the factors which (*a*) precipitate coma, (*b*) the speed with which coma may develop and (*c*) the manner in which the early symptoms are manifested Also, we must make earlier diagnoses, provide adequate therapy and safeguard against overtreatment if this complication is to be prevented, and corrected with minimum risk if it is already established

Patients should be aware of the benign course which controlled diabetes pursues and the upheaval that can come with great rapidity with

TABLE 1

A GUIDE TO AID IN CHANGING THE RESPECTIVE INSULIN PROGRAMS IN THE EVENT OF ACUTE COMPLICATIONS

(Further adjustment in the insulin dosage is indicated by the degree of glycosuria in succeeding six hour urine fractions on the new regimen)

Prior to Complication	During Complication
(1) No insulin	8—8—8—8 Regular insulin
(2) 40 Units p z insulin or 40 Units globin insulin	12—12—12—12 Regular insulin
(3) 80 Units p z insulin 12 Units crystalline insulin	25—25—25—25 Regular insulin
(4) 80 Units p z insulin 24 Units globin insulin	30—30—30—30 Regular insulin
(5) 96 Units p.z insulin 24 Units crystalline insulin (A M) 12 Units crystalline insulin (A M)	36—36—36—36 Regular insulin

an acute infection It is remarkable how many patients test the urine regularly for sugar only until they feel badly and, by discontinuing tests with the onset of a complication, deprive themselves of the only real clue that they understand, namely, strongly positive reactions for glycosuria Following in rapid succession come the anorexia, nausea and often vomiting The speed with which these patients may pass into the danger zone cannot be overemphasized

With adequate training diabetic patients make provisions for testing the urine in the event of illness and they will always regard loss of appetite with or without nausea in the presence of strong reactions for glycosuria as danger signals concerning the correction of which their physician should be consulted Also, the patient should know that in the anorexia

phase insulin must not be omitted if strongly positive reactions for glycosuria are present The pre-coma state should be suspected under

TABLE 2

ILLUSTRATIVE LIQUID DIET IN FOUR EQUAL FEEDINGS USED IN TREATMENT FOR ACUTE COMPLICATIONS OF DIABETES

Diet Prescription Protein 110 Gm , Fat 65 Gm , Carbohydrate 250 Gm , and Calories 2000

	Household Measure (Approx)	Grams	Protein	Fat	Carbohydrate
9 A M					
Cooked cereal	½ cup	120	3	—	15
Lactose, or sugar or dexin	1 tbsp (rounded)	18	—	—	18
Milk, whole	1 cup	240	8	9	12
Eggs, coddled	2	100	14	10	—
Prune juice	½ cup scant	100	—	—	18
			25	19	63
3 P M (Repeat at *9 P M* with suitable substitutions)					
Soup: Meat puree	1½ oz	45	10	4	0
Soup: Vegetable 18% puree	½ cup	100	5	—	18
Soup: Vegetable 9% puree	¼ cup	66	2	—	6
Soup: Vegetable 3% juice or puree	½ cup	100	2	—	3
Soup: Butter	1 tsp	5	—	4	—
Grapefruit juice	5 oz	150	—	—	14
Milk, whole	1 cup	240	8	9	12
Lactose, or sugar or dexin	2 tsp	10	—	—	10
			27	17	63
3 A M					
Milk, skimmed	2 cups	480	16	—	24
Eggs	2	100	14	10	—
Cream	1 tbsp	15	—	3	—
Lactose, or sugar or dexin	2 tsp	10	—	—	10
Grape juice	5 oz	150	—	—	27
			30	13	61

Suitable concentration of diets high in protein content may be maintained by utilizing nutragest, protenum, essenamine, and skimmed milk powders

(After G G Duncan, The Management of Diabetes Mellitus, The American Practitioner, *3* 139–151 [Nov] 1948)

these circumstances In case this suspicion is confirmed by a 4 plus reaction for glycosuria and acetonuria and a 1 or 2 plus reaction for plasma acetone, small frequently administered doses (every four hours)

of regular insulin are indicated The amounts are regulated according to the changes in the degree of glycosuria In these instances the ad-

TABLE 3

A TYPICAL DIET AS EMPLOYED WHEN THE DIABETES IS COMPLICATED BY ACUTE MEDICAL OR SURGICAL COMPLICATIONS

Diet prescription Protein 110 Gm , Fat 65 Gm , Carbohydrate 250 Gm , and Calories 2000

	Household Measures (Approx.)	Grams	Protein	Fat	Carbohydrate
9 A M					
Fruit 12%	1 lg serv	150	—	—	18
Cereal	½ cup	120	3	—	15
Eggs	2	100	14	10	—
Bread	1 sl	30	3	—	15
Butter	2 tsp	10	—	8	—
Milk, skimmed	1 cup	240	8	—	12
			28	18	60
3 P.M (Repeat at *9 P M* with suitable substitutions)					
Meat lean	1½ oz	45	10	4	—
Vegetable, 18%	½ cup	100	5	—	18
Vegetable, 6%	½ cup	100	2	—	6
Bread	1 sl	30	3	—	15
Butter	1 tbsp	15	—	12	—
Milk skimmed	1 cup	240	8	—	12
Fruit, 12%	1 serv	100	—	—	12
			28	16	63
3 A.M					
Milk, skimmed	1½ cup	360	12	—	18
Egg	1	50	7	5	—
Cottage cheese*	1 oz	30	6	—	—
Saltines	2	6	1	1	4
Butter	2 tsp	10	—	8	—
Fruit or juice, 12%	1 serv	100	—	—	12
Banana	1 lg	150	—	—	30
			26	14	64
Total for 4 meals			110	64	250

* Or cheddar cheese, 1 oz and no butter

(After G G Duncan, The Management of Diabetes Mellitus The American Practitioner, 3 135-151 [Nov] 1948)

ministration of salty broth by mouth will usually alleviate the nausea and permit frequent administration of carbohydrate by mouth which,

with the accompanying insulin therapy, will quickly correct the early ketosis Too little attention has been given to the value of sodium chloride in dealing with the pre-coma state

In the event that the acute complication which is precipitating the ketosis is not correctable promptly—within a matter of hours—the danger of ketosis can be reduced and the control of the diabetes can be more exactly regulated by prescribing the diet in four equal feedings—one every six hours—and regular insulin—one-fourth of the former total insulin dosage plus a modest increase—before each feeding, making adjustments according to the effect on the glycosuria in the respective six hour fractions We have used and advocated this principle of treatment since 1937 [1] It has received widespread acceptance [2, 3, 4] Illustrative insulin regimens are presented in Table 1

A liquid diet divided into four equal feedings which has been found to be satisfactory is presented in Table 2 When regular foods are tolerated a diet as illustrated in Table 3 may be employed until the routine diet and insulin may be resumed after the acute complication has subsided

CASE REPORT

The case report of a patient treated recently for diabetic coma is presented It illustrates many of the features already touched upon in this communication and others that will be dealt with in chronological order

E D , a Negress, aged 36 years, was admitted in a profound coma to the Pennsylvania Hospital on March 4, 1949 Relatives stated that the patient was three months postpartum and that since the delivery and following a "cold" she had complained of excessive thirst and appetite, and the frequent passing of large amounts of urine, and that she had lost weight from 111 kg (246 lb) to 96 kg (211 lb) in this period The family doctor had made the diagnosis of diabetes one week before her admission but his advice to seek hospital care went unheeded The patient had no appetite for food on the day prior to admission and toward evening she had "difficulty getting enough breath " At 4 00 A M on the day of admission she was found to be unconscious and could not be aroused

On admission a catheterized specimen of urine gave 4 plus reactions for glycosuria and acetonuria and there was a 4 plus reaction for plasma acetone The criteria for diabetic coma being fulfilled, insulin was given at once—50 units of regular insulin intravenously and 50 units of regular insulin subcutaneously Also, an intravenous infusion of normal saline was begun Chemical studies of the initial specimen of blood revealed a blood sugar level of 1452 mg per 100 cc and a CO_2 combining power of the plasma of 12 volumes per cent

The physical examination revealed the profound state of coma, marked obesity, a severe degree of dehydration, and typical Kussmaul breathing, also of a severe degree The tongue was red and dry and the conjunctival reflexes were absent The blood pressure was 95 mm Hg systolic and 50 diastolic, the pulse rate 136 and the body temperature 102 F (rectal) Otherwise the physical findings were not remarkable Her lungs were clear and there was no distention of the abdomen Laboratory findings summarized in Table 4 show

plasma sugar 1452 mg per 100 cc., plasma acetone 4 plus, CO_2 combining power 12 volumes per cent, blood urea nitrogen 38 mg per 100 cc, glycosuria and acetonuria 4 plus, albuminuria 2 plus, and many granular casts in the urine The leukocyte count was 17,650 per cu mm. of blood There were 5,080,000 red cells per cu mm, the hematocrit reading was 51 per cent and the specific gravity of the whole blood was 1 066

TABLE 4

SUMMARY OF LABORATORY DATA AND THERAPY (PATIENT E D)

Date	Blood						Urine		
3/4/49	Sugar mg./100 cc.	CO_2 vol., per cent	Acetone	Urea mg./100 cc.	Hematocrit per cent	Sp. Gr	Sugar	Acetone	Amount (cc.)
11 00 A.M	1452	12	++++	38	51		++++	++++	300
1 00 P.M	1372	16	++++		48	1 066	++++	++++	135
3 00 P.M	864	18	++++	34	38	1 059	++++	++++	700
5 00 P.M	834		++++		41	1 059	++++	++++	1125
7 00 P.M		33	++++		32		+++	++++	775
9 00 P.M	377		++++		35		+	++++	150
11 30 P.M	291		++++		35		0	++++	175
							First 12 hours		3360
1 30 A.M	287		+++		37		0	++++	150
3 30 A.M	324		++		35		+	+++	—
5 30 A M	251	49	+				0	+	—
9 00 A M	186		+	26	36		+	+	300
							Second 12 hours		450
							24 Hour Totals		3810

Total fluids administered First 12 hours 8,730 cc
Second 12 hours 3,000 cc
Total insulin administered First 12 hours 1,350 units
Second 12 hours 400 units

Management of the Case —*Insulin* —Insulin, with the exception of 200 and 100 unit doses administered early in the treatment, was given in doses of 50 units every half hour until the blood sugar was reduced to 377 mg per 100 cc The totals amounted to 1350 units in the first twelve hours of therapy and 1750 units in the first twenty four hours This amount of insulin far exceeds the quantity usually necessary to correct ketosis It will be observed in Table 1 that there are no evidences that excessive amounts of insulin were given nor were there, at any time, clinical signs of overdosage It was considered of utmost importance that large amounts of insulin be given frequently with ample carbohy-

drate as long as 4 plus reactions for plasma acetone were found As the concentration of plasma acetone decreases the sensitivity to insulin increases, hence a lessening of the amounts of insulin as well as a reduced frequency of administration are imperative if hypoglycemic reactions are to be prevented

Fluids—An extreme degree of dehydration was clinically manifest, the blood pressure was 95 mm of mercury systolic and 50 mm diastolic and the specific gravity of the whole blood was 1 066 (normal 1 052 to 1 058) These studies when repeated indicated that despite the administration of unusually great amounts of fluids—2700 cc of normal saline in the first two hours of therapy and 6200 cc in the first six hours—the specific gravity of the whole blood was still elevated—1 059 Nevertheless with progress being otherwise favorable the rate of the administration of fluid was sharply reduced The total volume of fluids—normal saline, plasma and glucose in distilled water—given in the first twelve hours reached a total of 8730 cc In the second twelve hours of treatment fluids given by mouth amounted to 3900 cc , bringing the total in the first twenty-four hours to 12,600 cc Less fluid in this latter period might have sufficed but with a urine volume of only 450 cc a smaller fluid intake was not justified Also, dehydration was still manifest The large urine output in the first twelve hours was not attributable to excess fluid intake but rather to the diuretic influence of the hyperglycemia which prevailed When this was alleviated the positive water balance was enhanced

Plasma—During the first hour of therapy the blood pressure decreased to a systolic pressure of 80 mm of mercury, the pulse rate became very rapid and eventually the pulse was imperceptible At this stage 350 cc of plasma were given A gradual increase in the blood pressure to 110 systolic and 70 diastolic ensued

Alkali—Because of the intensity of the air hunger 600 cc of sodium R lactate solution were given intravenously A dramatic improvement followed The administration of alkali doubtless accounts, to a considerable degree, for the elevation of the CO_2 combining power to 33 volumes per cent while the plasma acetone bodies, not so appreciably affected by this therapy, still gave 4 plus reactions This illustrates one means by which alkali therapy may, on the surface, be misleading

Glucose—The intravenous administration of 5 per cent glucose solution—700 cc—was begun eight hours after therapy had been started This was necessary as the blood sugar had been reduced to 291 mg per 100 cc while 4 plus reactions for plasma acetone still prevailed Subsequent carbohydrate intake was for the most part by the oral route

Potassium—Electrocardiographic tracings were made at the onset of therapy and frequently thereafter Selected tracings of the second standard lead are presented in Figures 262 and 263 The tracing taken taken on admission, Fig 262,*A*, shows a high T wave and a normal QT interval In contrast with later electrocardiograms the high T wave was interpreted as indicating a hyperpotassemia—a common finding prior

to insulin therapy and hydration in cases of diabetic coma A tracing 4 hours later (Fig 262,*B*) shows a reduction in the amplitude of the T wave The QT interval remained unchanged At seven hours (Fig 262,*C*) the T wave was still further depressed suggesting the early stages of hypopotassemia Potassium chloride, 1 gm , was given orally at once and repeated every four hours for five doses The amplitude of the T waves was normal (Fig 263,*A*) four hours after the onset of potassium chloride therapy and remained so (Fig 263,*B*) the electrocardiogram being repeated at twelve and twenty-four hours respectively

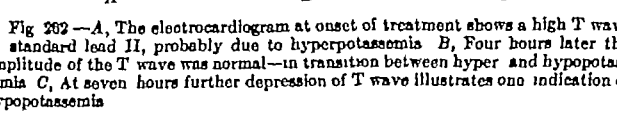

Fig 262 —*A*, The electrocardiogram at onset of treatment shows a high T wave in standard lead II, probably due to hyperpotassemia *B*, Four hours later the amplitude of the T wave was normal—in transition between hyper and hypopotassemia *C*, At seven hours further depression of T wave illustrates one indication of hypopotassemia

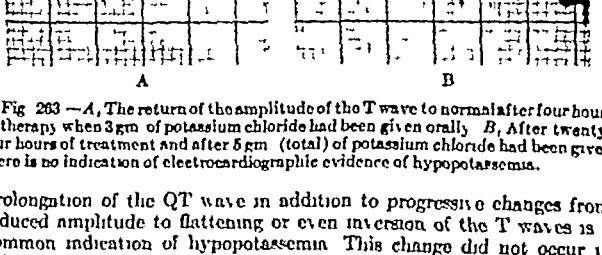

Fig 263 —*A*, The return of the amplitude of the T wave to normal after four hours of therapy when 3 gm of potassium chloride had been given orally *B*, After twenty-four hours of treatment and after 5 gm (total) of potassium chloride had been given there is no indication of electrocardiographic evidence of hypopotassemia.

Prolongation of the QT wave in addition to progressive changes from reduced amplitude to flattening or even inversion of the T waves is a common indication of hypopotassemia This change did not occur in this case Possibly the early detection and correction of the hypopotassemia prevented the development of this characteristic

In retrospect, and from the experience of others, formerly unexplained deaths in the second twelve hours of therapy in patients relieved of ketosis, and with no hypoglycemia, can surely be laid to hypopotassemia These patients despite their satisfactory blood sugar and CO

combining power levels were unduly weak and apprehensive and with a rather sudden onset of paralysis of the respiratory muscles death followed quickly Electrocardiographic tracings, taken frequently, afford an excellent means of detecting this dangerous complication hours before the clinical attack is likely to develop Holler's[5] patient developed paralysis of the respiratory muscles and was in a respirator several hours when a very low serum potassium concentration was found A dramatic recovery followed the administration of potassium chloride Electrocardiograms present a much simpler method of detecting this abnormality than does quantitative analysis of the serum potassium The work of Nadler and co-workers[6] has made this clear

The current explanation of the development of hypopotassemia is to the effect that during the intense dehydration potassium leaves the cells and increased tissue protein breakdown occurs and that hyperpotassemia results, but that when therapy is instituted the serum potassium is diluted, much is excreted with restoration of adequate hydration, cellular affinity for potassium is restored, and some is used in the glycogen deposition in the liver and in association with protein deposition in the tissues

Penicillin —Because of the unexplained fever, and of the prophylactic value of penicillin, this drug was given during the acute phase of the illness

Gastric Lavage —This measure was not made use of as there was no history of vomiting or abdominal pain and there was no distention of the abdomen An enema was given after consciousness was restored

Progress of the Case.—Improvements in the chemical values of the blood are noted in Table 4 Clinically the recovery was slower than is usually observed It was not until therapy had been carried out in an intensive manner for thirty-four hours that the patient was fully aware of her surroundings though after fifteen hours she gave indications of understanding what was said to her However, though in a semistupor she was able to take fluids by mouth after twelve hours of treatment and a liquid diet with values of 110 gm protein, 200 gm carbohydrate, and 95 gm fat (2100 calories) was prescribed and given in four equal feedings at six hour intervals The insulin also was administered at six hour intervals The diabetes was promptly controlled—fasting blood sugar value 86 mg per 100 cc —with the diet outlined above and with 180 units of insulin daily

There being no evidence of an acute complication remaining on March 11, the seventh day of therapy, a reducing diet—100 gm protein, 100 gm carbohydrate, and 22 gm fat (1100 calories)—with supplementary minerals and vitamins was allowed With this diet 110 units of insulin (80 units of protamine zinc and 30 units of regular insulin) daily maintained normal blood sugar values and freedom from glycosuria

Pursuing our oft repeated contention that an obese diabetic, and one who cannot attribute her obesity to insulin therapy, has a mild diabetes, and that obese patients are relatively insensitive to insulin, we did what one would not dare do in the case of a thin diabetic, we discontinued 110 units of insulin abruptly on March 17 and gave none thereafter Traces of glycosuria occurred on only four occasions during the remainder of her hospital stay—eight days—

and the fasting blood had increased only from 81 mg (March 17) to 143 mg (March 18) This patient was discharged on March 24 and when seen on the two succeeding weeks in the Out-Patient Department she had reduced in weight an average of 1 9 kg (4 lb) per week. The blood sugar values were normal, the last being 117 mg per 100 cc , and there was no sugar in any of the fractional urine collections

Comment.—This case illustrates the following

1 That even though the diabetes is mild an acute infection, even as mild as an upper respiratory tract infection, may precipitate a dangerous ketosis

2 That anorexia was an outstanding symptom of the ketosis and that it followed a period of excessive appetite

3 That a 4 plus reaction for plasma acetone accompanying a 4 plus reaction for glycosuria in a comatose patient verified the clinical diagnosis of diabetic coma before it was possible to know the blood sugar value and the CO_2 combining power of the plasma

4 That the rapidly deepening state of shock was ameliorated by the administration of blood plasma

5 That renal decompensation—indicated by the elevated blood urea nitrogen, the albuminuria and casts—developed with progression of the peripheral vascular collapse

6 That unusually large doses of insulin are tolerated during profound ketosis.

7 That many liters of fluid were indicated and that the administration was carried out rapidly while the need was great, using the specific gravity* of the whole blood as a reliable indicator—while the values were above 1 055 rapid administration was permissible but would not be considered essential if the blood pressure was well sustained and the hematocrit value was nearly normal More fluid, by far, was given to this patient than is usually the case

8 That a conservative amount (000 cc) of ⅙ molar lactate solution promptly alleviated the intense degree of hyperpnea and that despite this evidence of clinical improvement and an elevation of the CO_2 combining power to 33 volumes per cent a 4 plus reaction for plasma acetone still maintained This elevation of the CO_2 combining power is considered artificial and under these circumstances greater clinical value is placed on the qualitative—but crudely quantitative—reaction for plasma acetone

9 That glucose therapy was withheld for eight hours because of the severe degree of hyperglycemia It is not considered that glucose given earlier would have been harmful but that it was unnecessary is obvious

10 That hypopotassemia, which is prone to develop as treatment progresses, is detectable with adequate clinical accuracy by electrocardiographic studies and that this dangerous abnormality is readily cor-

* Determined by the falling drop method † A simple method† of determining this value using varying concentrations of copper sulfate solution has been widely used

rected by the oral administration of potassium chloride It is quite probable that the degree of diuresis influences the risk of hypopotassemia We suggest the routine use of potassium chloride, given by mouth, when renal excretion is good but withhold it in the event of oliguria or anuria unless there are electrocardiographic evidences of hypopotassemia If the urgency demands, potassium chloride may be given slowly intravenously—100 to 500 cc of a 1 14 per cent solution—or subcutaneously.

11 That the uncomplicated obese diabetic can tolerate large amounts of insulin—in this case 110 units—which can be abruptly withdrawn with minor elevation of the blood sugar resulting while the patient is receiving a low calorie diet which if continued brings the diabetes under perfect control

TREATMENT FOR DIABETIC COMA

Therapy is directed at the fundamental faults by giving insulin frequently and in adequate amounts, by restoring fluids and electrolytes until normal values prevail, and by providing adequate carbohydrate to permit a reduction in fat metabolism and to replenish depleted glycogen stores Other, but secondary therapeutic measures, are included in the following outline of treatment for diabetic coma employed at the Pennsylvania Hospital

OUTLINE OF TREATMENT FOR DIABETIC COMA

The working diagnosis of diabetic coma is made when 4 plus glycosuria, 4 plus acetonuria, and 4 plus plasma acetone are found in an acutely ill patient When these findings are present

I Begin treatment immediately
  INSULIN (regular)—40 units intravenously*
  60 units subcutaneously
  FLUIDS AND CHLORIDES—2000 cc normal saline are given (give rapidly, 15 to 20 cc per minute if systolic blood pressure is below 90 mg Hg)

II *Studies*—Secure immediately
  (1) Blood for sugar content, acetone bodies, hematocrit, CO_2 combining power, specific gravity (whole blood), and urea determinations
  (2) Urine for culture and routine complete analysis

III The Director of the Medical Division or, failing to reach him, a senior assistant will be notified promptly by the medical resident of the admission of a patient in diabetic coma The resident will also alert the Laboratory for emergency studies Also, arrangement for full time service of a resident and nurse should be made until the patient's life is out of danger

IV Secure *urine at two hour intervals*† for sugar and acetone determinations until the ketosis is corrected

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* With the exception of this initial dose all insulin is administered subcutaneously

† A retention catheter may be used for this purpose when necessary Utmost care should be taken to avoid introducing infection As a prophylactic measure

V Secure *blood* specimens at *four hour intervals, day and night*, for acetone, CO_2 and sugar and specific gravity (whole blood) *until the patient is conscious and retaining nourishment by mouth.* Subsequent studies as conditions indicate

VI Secure an electrocardiogram* as early as is practicable and repeat at four hour intervals for twenty four hours. More frequent tracings are indicated to guide therapy in cases of hypopotassemia.

VII *Treatment During Critical Phase Subsequent to the Preliminary Measures Outlined in I*

Immediately upon receiving confirmative reports on the blood sugar value and the plasma CO_2 combining power, or within one hour of making the diagnosis, whichever is earlier, begin

Insulin (regular) 50 units subcutaneously at one half hour intervals until an appreciable reduction of the plasma acetone or increase in the CO_2 combining power is noted Increases above these amounts will rarely be necessary but if no decrease in plasma acetone or increase in CO_2 combining power of the blood plasma has occurred after six hours† of therapy each succeeding dose may be increased by 25 units until such changes are noted Dangers of a rapidly developing hypoglycemia will be avoided by giving glucose (1 liter of 5 per cent solution) intravenously after four hours of therapy (see Par X) or carbohydrates orally if practicable

VIII *When to Reduce Insulin*

An appreciable reduction of the plasma acetone and an appreciable increase of the CO_2 combining power of the blood plasma coincide with a lessening of the resistance to insulin Such findings should put the physician on the alert to the possibility of a rapidly developing hypoglycemia When the clinical condition and laboratory findings indicate that the patient is showing satisfactory progress the insulin dosage schedule on an hourly and later two or three hour basis may be guided as follows

4 plus glycosuria—30 units
3 plus glycosuria—reduce to 20 units
2 plus glycosuria—reduce to 10 units
1 plus glycosuria—omit dose
0 glycosuria—omit dose of insulin and give 20 gm carbohydrate

The reduction of plasma acetone to a trace or an increase of the CO_2 combining power to a value above 40 volumes per cent is, if the clinical condition of the patient permits, indication for insulin and diet at six hour intervals (see Par XIII)

IX. *Fluids and Salts*

Loss of electrolytes and fluids to a marked degree occurs in the development of diabetic coma. Correction of these deficiencies at the earliest

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procaine penicillin 300,000 units, is administered intramuscularly and repeated in twenty four hours Immediately prior to removal of catheter a urine specimen for culture is obtained

* If indications of hypopotassemia are not corrected promptly by the oral administration of potassium chloride give 100 to 200 cc of a 1 14 per cent solution intravenously slowly until a satisfactory electrocardiographic response is observed

† It is usual to find little change in the blood findings in the first four hours but by the end of six hours improvement should be noted unless unusual circumstances are present

opportunity is imperative This is done properly by the administration of physiological saline solution, in amounts of 2000 to 3000 cc within the first two hours of treatment Further administration is given freely while the specific gravity of the whole blood remains above 1 055, while hematocrit values remain above 50 per cent and the systolic blood pressure remains below 90 mg Hg As soon as the patient's condition permits, broths and later carbohydrate containing fluids—strained cereal, gruel, ginger ale (noneffervescent) sweetened tea and later fruit juices—may be given Potassium chloride, 1 gm every four hours for five doses, is given routinely to the adult patient after eight hours of therapy, provided urine is being excreted freely Relatively smaller amounts are given to children Accurate records of fluid intake and output are essential

X *Carbohydrate*

Glucose, 1000 cc of a 5 per cent solution in normal saline, is given intravenously beginning four hours after the first dose of insulin was given, if at this time liquids given orally are not retained This is repeated in six hours if the patient is not taking or retaining nourishment by mouth

XI *Alkali*

The administration of alkali usually is not necessary However, an amount of racemic sodium lactate sufficient to raise the CO_2 combining power to a relatively innocent level—30 volumes per cent—will relieve air hunger rapidly Larger amounts are contraindicated The foregoing amount of alkali is permissible, also, for the critically ill patient having a plasma CO_2 combining power below 15 volumes per cent A transfusion using whole blood is an efficient means of restoring both base and blood volume

XII *Gastric Lavage—Enema*

The stomach should be emptied of its contents in cases of abdominal distention, abdominal pain, or vomiting Eight ounces of warm normal saline solution are left in the stomach An *enema* is indicated in nearly every case of coma It may be delayed until improvement in the patient's condition is noted

XIII *Diet*

When evidences of acute ketosis have subsided, a liquid diet is allowed for twelve to twenty-four hours and thereafter a "house diet" of the same values for example, protein 110 gm , fat 65 gm , and carbohydrate 250 gm (2000 calories) The diet is given in four equal feedings, one every six hours, and finally, with complete recovery from the attack, the diet and insulin regimens as for the uncomplicated diabetic patient are resumed

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PRACTICAL CONSIDERATIONS IN THE CONSERVATION AND REPLACEMENT OF BLOOD IN SEVERE HEMORRHAGE

LEANDRO M TOCANTINS, M D *

From this circumstance that the disposition of the blood to coagulate is increased as the animal becomes weaker, we may draw an inference of some use with regard to the stopping of hemorrhages, viz not to rouse the patient by stimulating medicines, nor by motion, but to let that languor or faintness continue, since it is so favorable for that purpose, and also that the medicines likely to be of service in those cases are such as cool the body, lessen the force of circulation, and increase that languor or faintness For in proportion as these effects are produced, the divided arteries become more capable of contracting, and the blood more readily coagulates, two circumstances that seem to concur in closing the bleeding orifices —Hewson, W Experimental Inquiries into the Properties of the Blood London, 1772, Volume 3, page 63

A hemorrhage may be considered severe when blood has been lost at such a rate as to cause symptoms indicating a serious upset in the ratio of blood volume to vascular capacity

Grading the severity of a hemorrhage on the basis of the amount of blood lost has a limited application and meaning, since relatively small losses may have a profound effect in patients whose blood volume or circulation has been impaired by other causes, while in most instances, no reliable estimate can be made of the amount of blood lost from accounts given by the patient or the family Whenever possible, as for example during an obstetrical delivery or a surgical operation, measurement of the extravasated blood enables the operator to forestall circulatory collapse by adequate blood replacement Generally speaking, however, a patient will display disturbing symptoms when an amount of blood equivalent to 1 to 2 per cent of his body weight has been lost within twenty-four hours

The remarks that follow are intended to stress a few broad principles and useful points in the management of these patients Insofar as possible, emphasis shall be placed on simple, easily accessible methods for the clinical recognition and control of altered physiological states In clinical practice, the nature of the problem and the circumstances and urgency of the situation seldom allow or warrant the use of more complex quantitative methods

When confronted by a patient giving a history or showing the signs of a severe hemorrhage, the physician should

1 Conserve the blood remaining in the body by reducing or checking further loss and devising ways to use blood still in the circulation to the greatest advantage

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2 Make a rapid estimate of the urgency and extent of the need for blood replacement and decide *how much* and *how fast* blood (or other fluids) is to be given
3 Maintain the patient under close observation and aid him in correcting any systemic defects in hemostasis, or other dysfunctions that he may have developed

MEASURES FOR THE CONSERVATION OF BLOOD

Patients who are bleeding should be put at rest, in a posture adjusted to minimize the hemorrhage and, whenever possible, have the bleeding area compressed by a suitable device or dressing

Rest.—Since extrinsic or intrinsic forces acting on the vessels may start or maintain bleeding in persons with or without defects in hemostasis,[1] efforts should be made to remove or attenuate those forces For example, if there has been bleeding from the tongue, the patient should be told not to talk for several hours after the bleeding stopped, movements of the tongue may cause bleeding to recur Anything that may exert a stress on the bleeding area should be avoided It may be advisable, if the wound is accessible, to splint the part or reduce its activity in order to keep the lips of the wound together Forcible manipulation or palpation of parts neighboring a bleeding area is hazardous

Posture.—This must be adjusted with two principal objectives (1) reduction of the flow of blood to the bleeding area and (2) maintenance of a blood supply to the brain and other important viscera with the blood remaining in circulation The type of posture indicated during a phase of bleeding depends chiefly on the region and system involved

1 Bleeding into the *brain*, *eye* or *ear* Head and shoulders raised slightly above the level of the trunk, abdomen and lower extremities horizontally
2 Bleeding from the *scalp*, *face*, *nose*, or *mouth* During waking hours, patient to sit up in bed, the trunk almost at right angles with the hips At night, body tilted slightly back The horizontal posture should be avoided, except during circulatory collapse
3 Bleeding from the *throat*, *pharynx*, *larynx* and *lower respiratory tract* Head and body flat in bed, with the head turned sidewards Sometimes it may be advisable to have the head lower than the shoulders, to allow the extravasated blood to escape from the mouth, and not go down to the trachea
4 Bleeding from the *gastrointestinal* or *urogenital tracts* Flat in bed In massive uterine bleeding, the lower half of the body should be elevated by inserting blocks under the legs of the bed or placing pillows under the hips and legs of the patient
5 Bleeding from the *extremities* The arm or leg should be raised and all constricting clothing removed

Tourniquets.—If the bleeding area is below the upper fourth of the extremity, a tourniquet or cloth constricting device may be used for the *temporary* arrest of the bleeding. When using tourniquets for this purpose, the following points should be observed

1 Apply the tourniquet (preferably a broad inflated circular bag) so as to exert just enough pressure to obliterate the pulse at the wrist (10 to 20 mm of mercury above the systolic pressure)[2] Before application, elevate the limb to drain most of the blood out of it, then quickly apply constriction to the specified level Note color of the skin below the tourniquet, if enough constriction is being applied, the skin distal to it should become paler and cooler than that on the proximal side If the skin is redder and warmer than above the tourniquet, constriction has been insufficient to shut off arterial blood flow

2 Check the pulse at frequent intervals, if blood pressure has risen after initial application of the tourniquet, the constriction must be readjusted If there is free bleeding, the amount of constriction may be adjusted to that required to check the bleeding

If the hemorrhage is in the foot or lower part of the leg, the tourniquet should be applied to the middle of the leg If the bleeding is from the hand or lower part of the forearm, the tourniquet should be applied to the middle part of the forearm Circular constriction applied around the base of the head, above the level of the ears and eyes may be effective in controlling, temporarily, bleeding from scalp wounds

3 At the most, a tourniquet should not be left on over one-half hour It is preferable to release it after a period of about ten minutes The release should be done *slowly* while watching for the appearance of bleeding This is to prevent pressure in the vessels from rising too suddenly, with consequent expansion and perhaps reopening of severed vessels If bleeding recurs when the tourniquet is partially released, it should be rapidly reapplied for another period of ten minutes or thereabouts Sometimes, repeated applications and slow releases will bring about hemostasis by alternately flooding the severed vessels and allowing the blood to stagnate within them, and a clot to form and harden It is important that the application be rapid and the release slow, to bring about this effect

If the location of the bleeding makes application of tourniquets necessary, steps should be taken to treat the wound as soon as possible so that the tourniquet may be removed Excessive prolonged constriction in any part of the arm, the lower third of the thigh, or that part of the leg just below the knee should be avoided because of the chance of injury to underlying nerves Pressure from a tourniquet may cause much pain and require sedatives to offset the effects of pain added to those of hemorrhage

Compression Dressings.—Tourniquets may be supplemented or at times replaced by the use of compression dressings which have the advantage of being free of the hazards of the tourniquet One such dressing proposed during World War II was simple and effective[3] It consists of a spongelike pad having enough resiliency to yield somewhat to the blood pressure, thereby permitting the circulation to continue through uninjured vessels to the tissues around and beyond the wound The dressing is intended not to stop the hemorrhage but to convert it to a slight ooze, which helps permanent hemostasis Resilient pressure dressings

eliminate edema, the formation of pockets and crevices, the collection of hematomas, besides affording protection from surface contamination The wound is splinted, and the rest afforded to it allows healing to proceed undisturbed

In using compression to arrest bleeding, the error is commonly made of applying excessive pressure Though it is difficult to adjust this pressure to the ideal degree (the amount required just to blanch the superficial vessels), tightly applied dressings or packs should be avoided

Peripheral vasoconstriction is among the most effective natural reactions of the body to conserve blood Besides helping the arrest of bleeding by reducing the caliber of vessels and the flow of blood within them it brings total vascular capacity down to within the limits of the diminished blood volume It is well, however, to help keep this vasoconstriction in the extremities, where ischemia can be tolerated better and longer than in organs like the liver, kidney, heart or brain Lowering the head and chest, applying compression bandages to the extremities and lower abdomen, raising the legs above the heart level are simple measures which help to maintain those central organs supplied with blood, at a time when there is a shortage of it in the circulation Heat should not be applied to the body at this time, since it will produce vasodilation, increase vascular capacity, accelerate metabolism and thereby aggravate the existing deficit of blood volume

Compression of Accessible Vessels.—Direct compression over a main arterial branch supplying the bleeding area is sometimes effective

In scalp wounds most of the bleeding comes from branches of the temporal and occipital arteries The *temporal* artery can be compressed just anterior to the upper part of the ear The *occipital* artery may be compressed in its course from the tip of the mastoid upward towards the occipital protuberance The blood supply to the scalp may be temporarily shut off by a band encircling the head passing over the forehead, above the ear, to the base of the skull and then upward just above the other ear to the forehead again Pressure on the *facial* artery can be exerted as the vessel crosses the body of the jaw just in front of the masseter muscle The *coronary* arteries supplying the lips may be compressed by pinching the lip between the forefinger and thumb

Neck wounds involving the large vessels usually affect both arteries and veins, bleeding from them is best controlled by direct pressure with the finger on the wound The *carotid* arteries may be compressed by pressure on the *common carotid* against the transverse process of the sixth cervical vertebra To exert pressure on the *subclavian* artery, the shoulder is raised slightly to relax the cervical fascia and the compression is exerted against the first rib, behind the middle of the clavicle This should stop the blood flow to the entire upper extremity The *brachial* artery may be compressed against the middle of the humerus The *radial* and *ulnar* arteries are compressible only at the wrist, just above the hand, bleeding from these arteries may be controlled by direct pressure on the wound, by a tourniquet about the arm or compression of the brachial and subclavian arteries The arteries of the palm of the hand may be compressed by grasping firmly a round body like a billiard ball or apple, and bandaging the hand tightly in this position Bleeding from the fingers can be controlled by constricting the *digital* arteries above the wound

The *femoral* artery may be compressed in the middle of the groin against the pubic ramus, much pressure may be needed for this purpose. The artery may be compressed lower down in the thigh against the shaft of the femur, this is best done with a tourniquet for a short period of time The *popliteal* and *tibial* arteries are difficult to compress Flexing the knee forcibly on a pad and holding the pad in place by a cross piece pressing forcibly against the popliteal space may be tried, the cross piece in turn being held in place by a bandage around the flexed leg Compression of the *dorsal* and *plantar* arteries can be best exerted by direct pressure on them or by compressing the *tibial* and *peroneal* as they cross the ankles. On the surface of the trunk the arteries most likely to be the source of serious hemorrhage are the *internal mammaries*, the *intercostals* and the *deep epigastric* In an *open* wound, bleeding from these vessels can be temporarily controlled by direct pressure with the finger or gauze packing

When using direct vascular compression to arrest bleeding, the same general precautions mentioned with reference to tourniquets should be kept in mind, expecially the need for *slow* decompression

THE REPLACEMENT OF BLOOD LOST

Assessment of the Need and Urgency for Blood Replacement.—The level of the arterial blood pressure is probably the most reliable single index to the need and urgency for blood *after* a hemorrhage If the pressure is under 100 mm of mercury, there are signs of circulatory collapse and the patient is known to have lost at least an amount of blood equivalent to about 1 per cent of the body weight, that amount should be given, but any additional transfusions should be withheld until there is a chance to observe the patient further and to note whether the pressure rises or the bleeding stops A rise of 10 to 20 mm of mercury is usually obtained in adults for each 500 cc of blood transfused if bleeding has ceased In order to attain a blood pressure of 100 mm of mercury or over, it is necessary to transfuse about 50 per cent of the calculated blood loss [4] If the pressure is slightly under 100 mm , the estimated blood loss is about 500 cc., the patient's skin is warm, and there are no symptoms of circulatory collapse, it is perhaps best not to transfuse but to keep the patient under observation, unless he is to be moved or to submit to surgical procedures involving additional trauma and blood loss Excessive zeal in transfusing is as objectionable as failure promptly to appreciate its need and carry it out Overfilling of the circulation in those already debilitated by injury or disease may precipitate pulmonary edema and other signs of circulatory embarrassment

If the blood pressure is under 50 mm , blood should be given at a rate of 20 to 40 cc per minute As the pressure rises to 70 to 80 mm the rate should be slowed to 10 to 15 cc per minute When the pressure reaches 100 mm or over, the rate of injection should not exceed 6 cc per minute A high arterial blood pressure in *itself* may not predispose to excessive bleeding, *provided the vessels and the rest of the hemostatic forces are unimpaired* Maintenance for a short time of a slight amount of pressure in the injured vessel is perhaps desirable, to assure some flow of blood from which the elements are separated which help close the wound [4]

When frequent blood pressure determinations are not practical, the quality (not the rate) of the pulse as felt by an *experienced* observer is probably the simplest guide A "thready" not easily compressible pulse indicates a high systolic blood pressure with probably a narrow pulse pressure An easily felt (or "full") pulse, resistant to compression, indicates a high systolic pressure with a fairly wide pulse pressure *A "bounding" easily compressible pulse means a lower systolic pressure with a wide pulse pressure, it is the type of pulse often felt during the stage of impending circulatory collapse after hemorrhage* A "thready" easily obliterated pulse signifies a drop in both systolic and diastolic pressure, and is observed during circulatory collapse If a "bounding" easily compressible pulse becomes imperceptible when the patient is propped up or the head of the bed is raised, it nearly always means that the patient is at the brink of circulatory collapse He is barely able to maintain compensation when lying flat, and develops hypotension and may faint when his posture is changed In judging the tension and compressibility of the pulse, much depends on the experience of the observer and his ability to make allowance for thickness of the skin, sclerosis of the vessel wall and position of the part, besides knowledge of any pre-existing disease in the patient

When about 20 per cent of the entire blood volume has been lost, the systemic blood pressure may begin to fall, thereby automatically reducing the rate of blood loss Unless forced by urgent reasons to act otherwise, it is sometimes advisable, especially in well hydrated young adults, at first to take advantage of this moderate hypotension (70 to 90 mm of mercury) which gives the hemostatic forces in and about the bleeding area a "breathing spell," or a chance to act without disruption Blood transfusions (especially when given rapidly) or other attempts to stimulate the circulation occasionally result in resumption or accentuation of the bleeding This is more likely to happen in older patients with arteriosclerosis and a defective hemostatic plug, or those who, though bleeding, have maintained a normal or high blood pressure These remarks do not apply to patients who are in shock or whose bleeding is chiefly due to a disorder of hemostasis (e g hemophilia) Prompt replacement of blood lost is indicated in these patients, especially when the hemorrhage has been severe and shows no sign of abating Their defective hemostatic mechanism gives no assurance that they may profit from such a short period of hypotension, furthermore, they tolerate rapid overfilling of the circulation even less than those without a systemic disorder of hemostasis

When blood or other fluids are being given, evidences of plethora should be looked for If concentrated protein (albumin) solutions are used, allowance must be made for their great osmotic power (25 gm of albumin in 100 cc are roughly equivalent to 500 cc of plasma) If, during an intravenous infusion, the patient's face becomes bluish and congested and the jugular veins are distended, the infusion should be discontinued Distention of the jugular veins should be looked for in

every patient receiving plasma or blood because of massive hemorrhage These veins are sensitive manometers of the pressure in the right auricle Filling of the jugulars in patients receiving blood is an indication that the blood is being dammed back of the right auricle, either because of cardiac failure, excessive blood volume or both *In any case, a surplus of blood already exists and no more should be given*

In unconscious or anesthetized patients, the condition of the superficial veins (and especially of the superficial jugulars which are most easily observed) may be the only guide as to when this point has been reached In conscious persons, substernal oppression, abdominal or lumbar pain, breathlessness and anxiety may be experienced when the volume or the speed of the transfusions have been excessive It is obviously unnecessary to administer fluids until these symptoms are produced When this happens inadvertently, the fluids should be discontinued at once, or at least slowed, until it is decided whether or not the volume or rapidity of the injection was responsible for the symptoms

When attempting to place a needle in the arm or leg veins of patients in shock, compression by the tourniquet in order to distend the vein must be critically adjusted so that the pulse can be felt at the wrist at all times Patients in collapse often require lighter compression with tourniquets than normal individuals, since their blood pressure is already low The arm or leg should be placed in a dependent position to encourage distention of the veins, and the skin over them should be warmed with hot cloths About three minutes should be allowed to elapse after the tourniquet is applied, since during shock it may take that long or longer for the veins to become filled, because of venous spasm If, after about five minutes of repeated trials, it has not been possible to cannulate a vein, a needle should be placed in the sternal bone marrow[6, 7] and the blood transfused through that route At this stage, blood must be injected at a fairly rapid rate (at least 50 cc per minute), as long as the pulse cannot be felt and the systolic pressure is under 50 mm of mercury Once the patient has recovered from the collapsed state and blood pressure has risen to 80 mm or higher, a needle should be inserted in the vein and the rate of infusion reduced to not more than 8 cc per minute, or the needle kept open with a slow drip of physiological salt or 5 per cent glucose solution

The order of preference of the type of fluid to be employed in acute hemorrhage is whole blood, plasma, albumin, gelatin, 5 per cent glucose and physiological saline When there is little blood available, plasma may be used, but it cannot be depended upon to correct the blood deficit For every three pints of plasma given to a bleeding patient, one transfusion of 500 cc of whole blood should be given[4]

It is wise to avoid giving large amounts (over 5000 cc in twenty four hours) of citrated blood or plasma when combating massive hemorrhage, as from a peptic ulcer Since, because of the deficient circulation, kidney function is often impaired, there is little excretion of the injected citrate The anticoagulant may accumulate in the blood and by slowing coagula

tion interfere with hemostasis in the bleeding area Even though calcium spontaneously mobilized into the blood will help rapidly to offset this effect, the occasional administration of calcium (10 cc of a 25 per cent solution of calcium gluconate intravenously) may help to overcome a possible excess of citrate The danger of alkalosis from an excessive amount of sodium citrate has been found to be negligible [4] Indeed a large amount of citrate may aid in the correction of the acidosis which is not infrequent in hemorrhagic shock [4]

Whenever massive blood replacement for hemorrhage is necessary and the bleeding seems to continue, a transfusion of unmodified blood (direct blood transfusion) should be tried Unmodified blood occasionally succeeds in bringing about hemostasis when even fresh, citrated blood has failed (e g thrombopenic and thrombasthenic purpura)

Bleeding from the mouth, nose, rectum, vagina or operative wounds may appear during, and last for some time after a transfusion of incompatible blood If the patient is conscious, signs of an incompatibility reaction (pain in the back, dyspnea, substernal oppression, headache, pinched anxious expression, chills) usually precede or accompany the hemorrhage In anesthetized patients these signs may be masked Brisk bleeding in and around the operative field, appearing suddenly in a patient receiving a blood transfusion, should make the surgeon suspect an incompatibility reaction and lead him to discontinue the transfusion at once The first and sometimes the only external indications of an incompatibility reaction aside from hemorrhage may be the appearance of jaundice, oliguria or dark urine within twenty-four hours after a transfusion given during an operation

Failure of the blood pressure to respond to transfusion is due, most often, to continuation of the bleeding If the amount of blood needed to overcome hypotension seems to exceed the estimated blood loss, persistence of bleeding may be assumed, provided other causes for the hypotension (psychogenic, endocrine) do not appear likely

PREVENTION OF RELAPSES. CORRECTIVE AND SUPPORTIVE MEASURES

When a patient has recovered from shock, the chances are that he will lapse into the same state within the next few minutes or hours, especially if, because of his condition, it has been impossible to reach the source of bleeding The patient should therefore be constantly watched, a needle kept in the vein, and plasma, whole blood and intraosseous needles made available nearby His blood pressure should be frequently measured, until he has been out of the shocked state for at least seventy-two hours *He should not be left alone or with untrained attendants during this period* Provision, meanwhile, must be made for the possibility of repetition of the shock state If it reappears three or four times within a twelve hour period in spite of transfusions, it is wise to consider exploring the probable bleeding area, since blood is being lost faster than it is replaced, and there is little likelihood that it will stop without interference This, of course,

applies to bleeding from a definite locus as a peptic ulcer, and not to patients with disorders of hemostasis such as hemophilia, where the bleeding is too diffuse to be corrected by surgical means

If there is cyanosis, oxygen should be given Since the circulatory collapse may be helped by intravenous injection of adrenocortical extract, it is wise to administer it to patients who have not reacted to the usual measures The extract (20 to 30 cc) may be given over a period of three hours in 500 cc of 0 85 per cent sodium chloride containing 5 per cent glucose Desoxycorticosterone acetate (15 mg subcutaneously or intramuscularly) may be used afterwards, doses of 10 to 30 mg daily being maintained as long as there are signs of impending circulatory collapse Oliguria is common in hemorrhagic shock and, if persistent, urine flow should be helped with intravenous hypertonic glucose solutions, besides blood or plasma transfusion

The patient's nutritional requirements must be looked after Unless a gastrointestinal disorder interferes, he must be given an adequate diet, including fresh fruit juices Glucose solutions may have to be given parenterally to maintain caloric intake in those unable to eat Vitamin K (2 to 4 mg of menadione) and ascorbic acid (100 to 200 mg) by mouth or parenterally, daily, are useful supplements to be given to any patient during a phase of bleeding Since a rapid restoration of blood volume is essential in these patients, it is advisable that, whenever possible, they be encouraged to drink plenty of fluids With the tissues well hydrated, the entrance of fluid into the blood is accelerated, and there is less likelihood of renal insufficiency and oliguria

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THE MANAGEMENT OF MASSIVE GASTROINTESTINAL HEMORRHAGE

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Massive hemorrhage from the gastrointestinal tract is a medical emergency As is true in the case of other emergencies, time and lives may be saved by the use of a prearranged plan In common with other institutions, the Medical Service at the Pennsylvania Hospital has put into practice a plan which has proved of inestimable value in the assessment and subsequent treatment of these critically ill patients The plan is not entirely original We have borrowed freely from the experience and views of others It is not a rigidly fixed plan Sufficient flexibility is retained to meet the varying needs of each individual patient, and routine procedures are not included merely to conform to a preconceived pattern Perhaps its greatest asset is that it provides the resident physician with a guide to follow when confronted with this emergency and the attending physician with the information essential to a proper conduct of the case Such a plan has the additional advantage that because of its uniform approach, the results of newer methods can be more easily compared and better evaluated

DEFINITION

Massive hemorrhage may be defined as the sudden and rapid loss of blood in sufficient quantity to produce the physiologic changes that are characteristic of shocklike states The amount of blood loss necessary to produce these changes will vary according to circumstances For example, the sudden "amputation" of a pint of blood in an otherwise healthy individual will produce only minor readjustments that may be barely detectable, whereas the sudden loss of an identical volume of blood from a poorly nourished, dehydrated patient may be sufficient to precipitate severe clinical shock It has been stated that massive hemorrhage may occur without shock This is true only in so far as the clinical signs are concerned, but it should be emphasized that the clinical picture does not necessarily reflect the physiologic state In other words, the sudden loss of a significant quantity of blood will result in the operation of vascular shunts, hemodilution and the like—physiologic changes which characterize shock and its allied states regardless of whether the clinical signs of classical shock are evident

DIAGNOSIS

Massive hemorrhage into the gastrointestinal tract may originate anywhere from the oropharynx to the anus Successful management will

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depend upon determining with reasonable accuracy the site of the bleeding as well as the nature of the lesion The present cornerstones of accurate diagnosis are (1) the clinical history, (2) the physical examination, (3) the laboratory studies

History.—While this may have to be brief because of the condition of the patient, much valuable information may be gained from a few pertinent, well directed questions It has been estimated that approximately 90 per cent of massive hemorrhages into the digestive tract are due to bleeding peptic ulcer Whereas 25 per cent of patients experiencing massive bleeding from peptic ulcer may furnish no history of antecedent digestive disturbances,[1] the vast majority will admit to some characteristic symptom such as pain or vomiting Loss of appetite, loss of weight or loss of strength will, of course, be suggestive of malignancy An estimation of the duration of the bleeding frequently may be made from the clinical history The location of the hemorrhage may be suggested by the color and the character of the vomitus or the stools The vomiting of blood or coffee-ground material and the passage of tarry black stools are indicative of hemorrhage originating in the upper gastrointestinal tract The passage of red blood by bowel is typical of bleeding into the lower intestinal tract On the other hand, when bleeding is brisk and peristalsis active, the tarry stool characteristic of upper intestinal bleeding may be accompanied or replaced by loose, darkly bloody movements Even the nature of the bleeding lesion may be suggested For example, the pain of ulcer commonly disappears with the onset of massive hemorrhage Minor changes in appetite or digestive capacity preceding the hemorrhage may be the earliest hint of a malignant growth In those instances where no antecedent history of dyspepsia can be elicited, careful questioning as to the use of alcohol and a history of jaundice or ascites may be sufficiently fruitful to warrant a tentative diagnosis of disease of the liver, or previously noted bleeding tendencies may suggest a blood dyscrasia Finally, in an age in which examinations for life insurance and military service are the rule rather than the exception, specific information with regard to blood pressure and urinary findings may be had for the asking and provide a useful basis for comparison in estimating the severity of the hemorrhage

Physical Examination.—Notation of arterial pressure, pulse and pallor is of primary consideration The association of marked hypotension with an unusually rapid pulse is indicative of serious hemorrhage and shock On the other hand, a relatively normal pressure and only slightly elevated pulse rate must not be taken to mean that the condition of the patient is satisfactory Actually shock may be impending Examination of the tongue will shed light upon the degree of anemia as well as the state of hydration Light palpation of the abdomen may reveal the presence of well localized tenderness characteristic of ulceration or a mass suggestive of new growth The presence of ascites, jaundice, palpable liver, or spider naevi points toward hepatic disease and the possibility of bleeding from esophageal varices Examination of the gums,

lymph nodes, spleen may disclose evidence of one of the blood dyscrasias Finally, by a rectal examination it may be possible to identify a rectal mass or shelf, the presence of hemorrhoids, or confirm a history of tarry stools

Laboratory Examination.—These fall into two categories There are those the principal use of which is to assist in making a differential diagnosis, and those the main value of which is in the assessment of the physiologic disturbances resulting from the sudden loss of blood At first glance the number of the examination listed may seem large—twenty-one in all In actual practice, however, rarely does the indication exist for the use of all of these tests at one time Even so, the criticism may be lodged that the number is excessive, beyond the capacity of many laboratories, and that the information to be obtained is imperfect and frequently of questionable value In answer to these questions, it must be emphasized that much will depend upon how the information is used In our opinion, a major factor contributing to the complications of massive hemorrhage is the failure to assess properly the physiological state of the patient and his capacity to adjust to the loss of blood In the past, too much reliance has been placed upon the physical appearance and a few scattered hemoglobin determinations, and too little upon laboratory study carefully planned to ascertain not only the amount of blood lost but the reaction of the body to this loss It is not an uncommon experience to see a patient whose condition had been considered satisfactory suddenly slip into full-blown shock—shock that in many instances might have been anticipated well in advance with the aid of modern laboratory methods and perhaps even prevented if adequate measures had been instituted before the appearance of the obvious signs The schedule which follows is recommended as a systematic aid in the differential diagnosis and management of massive gastrointestinal hemorrhage

1 *Routine in all cases.*
   - Complete blood count
   - Hematocrit
   - Prothrombin time
   - Blood typing and Rh determination
   - Total blood and plasma volume estimation
   - Blood urea nitrogen
   - CO_2 combining power
   - Serum chloride
   - Urinalysis
   - Stool examination for color, consistency, and blood, both gross and occult
2. *In the absence of a definite history of dyspepsia or when there is the possibility of "liver spleen disease"*
   - Bromsulfalein dye excretion test
   - Cephalin flocculation test
   - Thymol turbidity test
   - Quantitative serum bilirubin
   - Urinary urobilin and bilirubin quantitative estimation

3. *In the absence of a definite history of dyspepsia or evidence of disease of the liver and when there is the possibility of hemorrhagic disease as the source of bleeding*
   Platelet count
   Bleeding time
   Coagulation time
   Clotting time and retraction (venous blood)
   Capillary fragility test
   Bone marrow study

The need for a *complete blood count, hematocrit,* and determination of *blood type* in every case requires no comment The *white cell count* normally rises fairly promptly in response to a massive hemmorhage A low count may indicate an inability of the body to respond to the stimulus because of pre-existing debilitating disease or anemia or it may suggest the possibility of "liver-spleen disease"

The *prothrombin time* has been included as a routine procedure because it is frequently below normal in massive hemorrhage and will emphasize the need for supplemental vitamin K therapy Marked depression, 50 per cent or below, should suggest significant liver disease A cursory review of the records of ten patients hospitalized with the diagnosis of massive hemorrhage from esophageal varices based upon x-ray study or postmortem examination failed to disclose a prothrombin level above 50 per cent of the normal control This number of cases is too small to warrant any general statement as to the critical level of prothrombin as a diagnostic index of bleeding from esophageal varices due to hepatic disease Unfortunately there were a number of other patients who died of proven hemorrhage from esophageal varices but in whom no prothrombin levels were obtained, possibly because these patients were admitted in extremis and the diagnosis was all too apparent The methods of reporting prothrombin levels vary We prefer a report which includes not only the seconds required for the clotting of the control and the patient's plasma, but in addition includes the level in terms of the percentage of the normal control as plotted upon a curve derived from the results of serial dilutions The graph obtained is not a straight line The significance of a few seconds difference may not become apparent until the values are plotted upon such a curve which will bring out more clearly the deviation from normal

The *flocculation tests* for liver function have been included because in every instance of massive hemorrhage from esophageal varices associated with hepatic disease they have been strongly positive, in contrast to bleeding from peptic ulcer unassociated with disease of the liver

We have found the *bromsulfalein test* such a simple and useful adjunct in differential diagnosis that it has almost become routine in all cases of hemorrhage The elimination of the dye is not significantly affected by the presence of anemia although cardiac failure may decrease its removal from the blood stream We commonly measure the amount of dye retained thirty minutes after the intravenous injection of 5 mg of bromsulfalein per kilogram of body weight Retention above 10 per cent is considered abnormal Since inaugurating this technic we have not accumulated a sufficient number of cases with hemorrhage from proven esophageal varices to establish a critical range However, White, Zamcheck and Chalmers[2] have recently described their experience with the bromsulfalein test as a diagnostic aid in massive gastrointestinal bleeding They report that the patient without liver disease shows only a moderate increase of dye retention or none at all either during shock or within an hour or two after recovery from shock, within twenty-four hours after recovery from shock the

excretion of bromsulfalein is normal in almost all instances The patient with liver disease, on the other hand, shows an elevated dye retention which is further increased during shock, even more than in the patient with a normal liver They conclude that a normal bromsulfalein excretion obtained during shock effectively excludes ruptured varices caused by cirrhosis as the cause of massive hemorrhage from the gastrointestinal tract. It is not infallible, however, and we have had the experience of receiving a normal report in the presence of strongly positive flocculation tests and other evidences of bleeding associated with advanced disease of the liver

It has long been recognized that the *blood urea nitrogen* levels may be of distinct value in following the course of bleeding into the gastrointestinal tract. The sudden introduction of a large quantity of blood into the upper intestinal tract is followed within eight to twelve hours by an appreciable rise in the blood urea nitrogen level Bockus[1] feels that the level of the urea nitrogen may be of prognostic importance The elevation may be roughly proportional to the amount of blood lost into the intestinal tract. With cessation of bleeding the level should be expected to return to normal within twenty four to forty-eight hours An elevation of the urea nitrogen may be due to the absorption of blood alone or to a functional renal impairment secondary to hypotension or dehydration, or it may be associated with a preexisting renal disease, or a combination of these. A figure in the neighborhood of 100 mg or more per 100 cc indicates a poor prognosis.

The *plasma* CO_2 and *chloride* studies may be helpful in elucidating which of the above mechanisms is the major factor and in conjunction with the *serum protein* and *albumin* determinations may serve as a guide in the choice and administration of fluids

In September 1938 Bennet, Dow, Landor and Wright[2] published in the Lancet an article in which they point out the advantages of determinations of circulating *red cell* and *plasma volume* in the assessment and management of severe gastrointestinal hemorrhage. They state "Hemorrhage occurs at the expense of both plasma and corpuscles, but whereas the body restores the lost plasma with considerable rapidity, it can only restore the lost corpuscles by a process of regeneration occupying weeks of time " It is the continuous dilution of red cells with plasma drawn from the tissue spaces which renders a simple red cell count or hemoglobin determination such unreliable indices of the extent of the bleeding It should be clear, as they state further, "that assessments based on hemoglobin estimations are liable to grave fallacy and that the error is made at moments of extreme importance, i e , in the hours immediately following a severe hemorrhage." For the same reason, dilution of blood by the reconstitution of plasma drawn from the tissue stores may make it impossible to be certain whether the hemorrhage has ceased or is continuing These investigators point out that the only reliable determination that will give a reasonably accurate indication of not only the amount of blood lost, but also the liklihood of continuing hemorrhage is an estimation of the circulating red cell volume In the case of a sudden massive hemorrhage, they have shown that a certain determinable volume of circulating red cells is "amputated" and if there is no further bleeding that the remaining volume will be maintained at a constant level

The accuracy of various methods of estimating plasma volume has been questioned on technical as well as theoretical grounds After an extensive experience Gregersen[3] has concluded that the error involved in the *dye method* of determining the circulating plasma volume "is negligible in comparison with the reduction of the blood volume observed in shock caused by trauma or hemorrhage " His

simplified method consists in measuring the plasma concentration of the dye T-1824 with the portable Nickerson Decade Photometer The total plasma volume is obtained from the dye concentration in a single blood sample drawn ten minutes after the intravenous injection of an ampule of a standard dye solution of known concentration By reference to a chart the plasma volume may be read directly from the photometer reading The total volume is calculated from the plasma volume and the hematocrit The entire operation should not take more than forty-five minutes Gregersen has summarized the advantages of this procedure as follows "Since the reduction of blood volume precedes the appearance of the symptoms of shock, it constitutes a valuable prodromal sign and the early determination of the blood volume may therefore be most useful as a means of predicting whether or not shock is impending With this information available, shock can be combatted before it develops Furthermore one can estimate the minimum amount of blood or blood substitute necessary to bring the patient out of danger of shock from reduced blood volume " We have recently had the opportunity to check the validity of this last statement as the following case history illustrates

Case I —A 28 year old white man, 68 cm tall, weighing 198 kg, was admitted to the Pennsylvania Hospital seven hours after a fainting attack and the passage of a tarry stool His general condition appeared good and his blood pressure was normal The hematocrit was 45 per cent Eight hours after admission a plasma volume estimation yielded the following information

Total blood volume	4,820 cc
Total plasma volume	2,940 cc
Total red cell volume	1,880 cc
Hematocrit	40 per cent

The average normal total blood volume calculated on the basis of actual weight before the hemorrhage was 7650 cc The blood volume had been thus reduced by approximately 37 per cent which placed the patient in the danger zone, although there were no signs of clinical shock Less than twenty-four hours after this determination and before intravenous infusions had been given, the blood pressure took a sudden drop with a concomitant rise in pulse rate A transfusion of 500 cc of whole blood was started promptly, following which a second blood volume estimation was made with these results

Total blood volume	4,936 cc
Total plasma volume	3,307 cc
Total red cell volume	1,629 cc
Hematocrit	33 per cent

Since approximately 225 cc of that total red cell volume represented that supplied by the transfusion, the actual loss between the two determinations was 476 cc of red cells which is roughly equivalent to slightly more than a liter of whole blood The passage of large tarry stools was noted During the next three days 2000 cc of whole blood were given before a third blood volume estimation revealed

Total blood volume	5,756 cc
Total plasma volume	3,281 cc
Total red cell volume	2,475 cc
Hematocrit	43 per cent

These figures indicate a return as a result largely of the transfusions of blood, to a total blood volume approximating 75 per cent of the average normal for the patient's weight The accuracy of these determinations is indicated by the

close agreement between final estimated red cell volume and what would be expected as the result of the infusion of 2000 cc of whole blood The estimated red cell volume before 2000 cc of whole blood was 1629 cc. The addition of 950 cc. of red cells from the transfusion should bring the total, provided there was no further bleeding, to a total of 2579 cc The estimated red cell volume after the transfusion was 2475 cc —a difference of only 104 cc

Criticism of the dye method in estimating plasma volume continues to appear in the literature Much of this criticism is justified if the method is to be used for an accurate quantitative measure of plasma volume changes In a study of patients exhibiting massive hemorrhage, where the plasma volume changes are relatively great, the errors inherent in the method assume negligible proportions from a practical clinical standpoint As Hopper and his co workers[5] have pointed out, the dye method is fairly reliable as a qualitative measure of relative plasma volume and consistently indicates correctly the direction of the change in the plasma volume, and can be used in a study of clinical shock provided the limitations are taken into account in interpreting the results Furthermore, Noble[6] concludes that "the reduction in plasma and blood volume in shock are so large in comparison to the error in estimating the amount of blood or plasma needed by the patient will seldom be serious " In employing the dye method for the study of massive gastrointestinal hemorrhage, we have encountered a number of other minor difficulties which should be mentioned Evans blue remains in the circulation for a relatively long period and may interfere with reading a bromsulfalein test. For that reason, if a bromsulfalein test is indicated it should be done first, as in this test the dye is eliminated rapidly and will not interfere with Evans blue The presence of lipemic material in the serum may interfere, on the other hand, with establishing an accurate end point with Evans blue The most common source of this material is the milk and cream diet of patients suspected of ulcer Substitution of fat-free milk or formula for a period of a few hours prior to carrying out the test will usually overcome this difficulty

A more practical method of estimating the degree of blood loss in acute hemorrhage has been developed by Green and Metheny[7], which is based on the cardiovascular response to tilting the body to an angle of plus 75 degrees for a period of three minutes They have concluded from their studies that an increased pulse rate on tilting of less than 25 beats per minute indicates negligible blood loss An increase of 30 beats or more above the supine rate indicates a transfusion requirement of approximately one liter, while the development of syncope indicates the need for about 1500 cc of blood The signs of shock in the supine position indicate a requirement of a transfusion of at least 2000 cc of blood

Urinalysis is frequently overlooked and its importance forgotten during the first few hours after the admission of a patient suffering from massive hemorrhage Much valuable information can be obtained from the examination of a freshly voided specimen of urine. Normal urinary findings indicate good renal function. Low specific gravity, albumin, casts will warn of possible preexisting renal disease. High specific gravity in association with a low pH, perhaps a trace of albumin, and a negative sediment indicates the strain of dehydration but suggest good functional capacity The maintenance of a twenty four hour urinary output of 1000 cc or more is an excellent index of success in combatting shock. The presence of bilirubin or urobilin in significant titers should arouse the suspicion of serious hepatic disturbance.

The importance of recording the *gross appearance and character of each stool*

that is passed should require no emphasis This observation is of particular value in those instances in which the signs of recent hemorrhage are present but the site of bleeding remains in doubt

PATHOLOGICAL PHYSIOLOGY

A brief review of the more important current concepts of the pathological physiology associated with massive hemorrhage may be helpful in understanding the rationale of the treatment subsequently to be presented. Every effort will be made to emphasize the importance of the invisible and usually unsuspected changes that occur in the liver, kidneys and adrenal glands These changes are generally considered to be secondary to prolonged hypotension and anoxia

Experimentally Wiggers[8] and others have shown that following the sudden loss of a significant quantity of blood there is an initial stage during which the body attempts reflexly by vasoconstriction to compensate for the reduced circulating volume by a corresponding reduction in the vascular bed, and by the mobilization of cells from certain depots, notably the spleen This may be shortly followed by a more gradual shift of plasma fluid from the surrounding tissue spaces into the systemic circulation Clinically this stage may be manifested by little else than pallor and perhaps slight hypotension If the patient is in a relatively good state of nutrition and hydration, and there is no further bleeding, compensation may be adequate and an uneventful recovery may follow If, on the other hand, the bleeding continues, the loss of blood may exhaust the capacity to compensate, in which case sudden decompensation or shock is likely

During the period of apparently satisfactory compensation characterized by nothing more alarming than pallor and perhaps slight hypotension, the function of the liver, of the adrenals and of the kidneys may be seriously impeded because of the shunting of blood away from these highly vascular organs in an effort to maintain an adequate circulating blood volume and pressure Trueta[9] has ably pointed out the shunting of blood away from the important functioning units in the cortex of the kidney during shock-like states Frank[10] and his associates likewise carried out experiments with regard to the role of the liver in massive hemorrhage in dogs, noting that vivi-perfusion of the liver during massive hemorrhage provides sufficient protection to produce survival while vivi-perfusion through the systemic veins does not They have concluded that the "preservation of liver function is of crucial importance in recovery from advanced hemorrhagic shock "

Wiggers and Ingraham,[11] in discussing the definition and diagnostic criteria of shock following hemorrhage, describe three major conditions that may develop from uncomplicated hemorrhage (*a*) A simple hemorrhagic hypotensive state characterized by a reduction in the total circulating blood volume following cessation of a hemorrhage of not more than 30 to 40 per cent Although recovery is almost certain without transfusion in such instances, withholding blood is not recommended in as

much as a suitable transfusion will promptly restore normal conditions. (*b*) An impending shock state in which the residual volume, after cessation of an uncomplicated hemorrhage, is less than 60 per cent of the normal prehemorrhage level If the blood volume is restored within an hour after the onset, before permanent tissue damage due to anoxia has occurred, recovery is likely (*c*) A terminal hemorrhagic shock state which is characterized by a persistent decline in the blood pressure to very low levels, rapid heart rate, passage of bloody fecal material, ultimate hemoconcentration and death due to irreversible tissue damage

It is unmistakably clear from the foregoing that the successful treatment of massive hemorrhage depends upon the prompt restoration and maintenance of an adequate circulating blood volume which is, in most instances, not less than 60 per cent of the normal prehemorrhage level It is equally clear that the early determination of the blood volume offers the most accurate means of evaluating the true physiological state of the patient who has suffered a massive hemorrhage since the reduction in blood volume may precede, by many hours, the symptoms and signs of shock

TREATMENT

Transfusion.—In the presence of *full-blown shock resulting from hemorrhage and characterized by a persistently falling blood pressure below 100 mm of mercury systolic and a steadily rising pulse rate above 100 per minute, prompt replacement of blood is indicated* In *impending shock the clinical signs may not be so obvious and yet the indication for transfusion is but little less urgent* It is in the latter case that an early blood volume determination has its greatest value since a reduction of more than 30 per cent from the normal prehemorrhage level indicates that the patient has entered into the danger zone and needs blood if shock is to be prevented The quantity of blood to be infused will vary with the condition of the patient A patient in full blown shock will require, in most instances, at least 2 liters of blood to replace that already lost, and more will be required to replace that lost by additional bleeding *The administration of blood should be continuous as long as the indications for blood persist regardless of the total amount involved* Sometimes the amount of blood that must be administered under these conditions is almost incredible.

Case II—A 41 year old Negro male was admitted to the Pennsylvania Hospital a short time after the sudden hematemesis of "one or two quarts" of bright red blood Initial blood pressure was 100/60, pulse rate 108, red cell count 2 1 million, hemoglobin 6 0 gm , and the hematocrit was 24 per cent During the ensuing twenty four hours this patient vomited or passed by rectum a measured total of 6200 cc of what appeared to be pure blood and clots During the same period he received a total of 7500 cc of citrated whole blood in addition to 4800 cc of 5 per cent dextrose and physiologic salt solution During this period the blood pressure fluctuated between a high of 120/80 and a low of 54/45 and the pulse ranged between 100 and 138 per minute Of greatest significance is the fact that his urinary output never faltered In the first twelve hours it was

recorded as 250 cc plus He was known to have passed more but the exact volume had not been noted During the next twenty-four hours he excreted 1250 cc of urine and this was followed by 1870 cc in the succeeding twenty-four hours The survival of this patient is attributed to the fact that in spite of the terrific blood loss, it was possible to maintain the circulating blood volume at levels sufficient to permit continued adequate function of the kidneys

A suggested guide to therapy is given in Table 1

TABLE 1

SUGGESTED GUIDE TO THERAPY

Clinical Findings	Laboratory Findings	Blood Transfusion
Stage I		
Blood pressure normal Pulse normal to slightly increased Tilt test negative	RBC 4 0 million plus Hemoglobin 12 0 gm plus Hematocrit 36 volumes per cent plus Blood volume 80 per cent plus of prehemorrhage level	Not indicated
Stage II		
Blood pressure normal or slightly depressed Pulse normal or slightly elevated Tilt test pulse increase to 30 beats or more	RBC 3 9–3 0 million Hemoglobin 11 8–9 0 gm Hematocrit 35–27 vol per cent Blood volume 70–79 per cent prehemorrhage level	Approximately 1000 cc
Stage III		
Blood pressure below 100 Pulse increased above 100 Tilt test syncope	RBC 2 9–2 25 million Hemoglobin 8 8–6 8 gm Hematocrit 26–22 vol per cent Blood volume 60–70 per cent of prehemorrhage level	Approximately 1500 cc plus
Stage IV		
Blood pressure 60 and below Pulse over 120	RBC 2 25 million or less Hemoglobin 6 8 gm or less Blood volume 60 per cent or less of prehemorrhage level	Approximately 2000 plus

Prompt restoration of circulating blood volume to prehemorrhage levels is a matter of utmost urgency in those patients whose total volume has sunk to 60 per cent of normal, as prolonged tissue anoxia associated with this degree of blood loss will result in irreversible changes incompatible with recovery While whole blood is the solution of choice, plasma is usually more quickly procured In critical cases, plasma infusion should be started at once and replaced by suitably matched whole blood as soon as the latter can be secured If neither blood nor plasma are immediately at hand, infusion of 5 per cent dextrose in physiologic saline solution may

be used as a temporary but very much less effective expedient until blood or plasma are obtained If veins are not readily available because of obesity, collapse or other cause, much precious time may be saved by giving the infusion through a sternal marrow puncture

The speed at which the infusion is administered will depend upon the clinical condition of the patient If the systolic blood pressure is 50 mm of mercury or below, the blood or plasma should be permitted to run in rapidly, as much as 500 cc in thirty minutes As the pressure rises to 100 mm or above, the rate of flow should be reduced to not more than 8 cc per minute A word of caution should be given with regard to the rapid installation of intravenous fluids Glucose and saline solutions are apt to produce pulmonary edema because of the low protein content of the diluted plasma Whole blood is less prone to produce this complication although it has been described as a consequence of rapid infusion of blood in experimental animals In one of our patients acute pulmonary edema developed during the course of an infusion of blood The important factor in this instance was an already seriously damaged circulatory system due to arteriosclerotic heart disease with advanced aortic stenosis and cardiac enlargement *The rapid infusion of any solution should be carried out with extreme caution and with continuous observation in any patient known or suspected of having a seriously damaged cardiovascular system* It must also be remembered that some patients who have suffered exsanguinating hemorrhage may exhibit cardiac irregularities and vasomotor collapse due to acute failure of the circulatory center If the disturbance has continued for a considerable time, it is conceivable that the damage may have become so severe that the cardiovascular system is incapable of handling a sudden and rapid increase in its load

On the other hand, Glasser and Page[13] carried out some provocative experiments on the production and treatment of hemorrhagic shock in dogs Under carefully controlled conditions they subjected the animals to a period of moderate hypotension, maintaining the systolic pressure at 50 mm. of mercury for ninety minutes This was followed by a period of drastic hypotension with the systolic pressure maintained at 30 mm for an additional forty five minutes The animals were then bled until the respirations and heart beats had remained arrested for a period of two minutes Then they rapidly replaced by *arterial transfusion* the blood that had been removed with the addition of 0 5 cc of 1 10 000 adrenalin solution per kilogram body weight Artificial respiration was carried out simultaneously and ouabain 0 05 mg per kilogram of body weight was given intravenously Eighty four per cent of the animals were successfully resuscitated, 51 per cent lived ten hours, and 33 per cent survived These experiments suggest that the heroic measure, that of arterial transfusion might be worth considering as an emergency procedure in some cases of massive hemorrhage of extreme degree, and in which acute circulatory failure has developed and is, as yet, of short duration.

While the transfusion of whole blood is the greatest single weapon available in the treatment of massive hemorrhage, it is not an unqualified blessing There is the risk of a reaction due to a hematologic incompati-

bility and the development of a lower nephron nephrosis syndrome For a patient whose kidney function may already be severely taxed, this added insult may be the turning point toward a fatal outcome *Extreme care must be exercised in obtaining compatible blood* If blood from more than one donor is to be given, *fresh* blood should be drawn from the patient and rematched with the prospective donor before each subsequent infusion This is recommended as an additional means of minimizing the chances of a reaction due to an unsuspected incompatibility arising from the previous transfusion As a further protection efforts should be made to maintain an alkaline urine During the transfusion and the ensuing twenty-four hours, each specimen of urine should be tested for pH as soon as voided If the urine is strongly acid or acidosis is suspected in association with dehydration, 200 to 500 cc of one-sixth molar lactate solution may be administered initially at the time of the transfusion Additional lactate will be indicated if the CO_2 combining power of the plasma is subsequently found to be depressed Nicholson[13] reports that 1 to 1½ liters will render the urine alkaline in patients with acidosis from severe infections, while approximately 500 cc twice daily will maintain alkalinity

Fluids.—It is important to maintain proper fluid balance with a total excretion of not less than 1000 cc of urine in twenty-four hours Renal function may be impaired because of preexisting diseases, dehydration, hypotension, or a lower nephron nephrosis syndrome In the absence of any contraindication such as vomiting, fluids are more safely administered by mouth and should be in the form of frequent, small, nourishing feedings If dehydration is severe and the oral intake is not sufficient to make up for the loss, hypodermoclysis of physiologic salt solution or 5 per cent dextrose solution may be given simultaneously with the blood transfusion In this way additional fluid is made available in the tissue spaces to be drawn on as needed, the danger of overloading the circulation and pulmonary edema is avoided, and last but not least, the veins are reserved for blood transfusions and necessary blood studies There will be times, however, when the need to correct the disturbed acid-base balance will demand the intravenous administration of fluids other than blood or plasma The choice of fluid will depend upon the direction and the degree of the disturbance of the acid-base equilibrium as indicated by the results of the blood chemistry determinations

Diet.—The principle of early feeding of patients with bleeding into the gastrointestinal tract has been generally accepted The food should be in small quantities, easily assimilated, and high in nutritional value At the Pennsylvania Hospital, as soon as the patient is able to tolerate anything by mouth, he is started on a regimen of hourly feedings of 3 to 4 ounces of a milk formula Four ounces of formula* every hour

* Liquid skimmed milk	1 quart	each ounce	Protein	2 8 gm
Cream 20 per cent	1 pint		Fat	1 9 gm
Powdered skim milk	8 oz		Carbohydrate	5 4 gm
Dexin	4 oz			
Eggs, raw	8			

from 6 A.M. to 10 P.M. will provide 190 gm. protein, 130 gm. fat and 365 gm. carbohydrate, calories 3390. The outstanding feature of this formula in addition to its high nutritional properties is its low cost.

Medication.—In the presence of active bleeding in patients suspected of having peptic ulcer, *antacids* should be avoided. The absorbable preparations carry with them the danger of producing serious disturbance of the acid-base balance especially in the presence of dehydration or vomiting. *The nonabsorbable preparations, principally the colloidal aluminum hydroxide gels, are avoided as they have been known to mix with blood and form a dense clotlike mass capable of producing intestinal obstruction.* Moreover, it is felt that if the patient is capable of taking anything by mouth it should be in the form of nourishment.

The oral administration of various forms of *protein hydrolysates* is now in vogue. We have not been convinced that the use of these preparations holds any distinct advantage in the vast majority of cases over a milk formula which is fortified by additional protein in the form of powdered skim milk. Surely a patient with peptic ulcer, by the very fact that he has such a disease, is capable of digesting protein and assimilating it without the aid of preliminary hydrolysis in the laboratory. Furthermore, recent studies at the Pennsylvania Hospital by Duncan and Waldron[14] indicate that the ingestion of fat increases the coagulation of blood to a marked degree—a distinct asset in the management of gastrointestinal bleeding.

For a *sedative* one of the soluble barbiturates such as sodium phenobarbital in dosage of 0.065 to 0.1 gm. (1 to 1½ grains) administered hypodermically is preferred to morphine inasmuch as the latter frequently induces nausea and vomiting.

Antispasmodics such as belladonna and its derivatives are avoided during the acute phases of bleeding because of their undesirable side effects.

Vitamins are given parenterally during the acute phases of bleeding and later by the oral route. The daily dose should include: vitamin K 2 mg., soluble vitamin B fraction containing thiamine 10 mg., riboflavin 10 mg., pyridoxine 50 mg., niacinamide 250 mg., ascorbic acid 200 mg. *Iron* is withheld until the stools have returned to normal color and then administered in the form of the ferrous salt in dosage of 0.6 to 0.8 gm. (9 to 12 grains) daily by mouth.

Cathartics are avoided. In the presence of distention and in the absence of shock, a small tap water enema may be helpful. Usually after a severe gastrointestinal hemorrhage the stools are soft. One or 2 ounces of mineral oil nightly is harmless and will aid in keeping the stools soft if there is a tendency to constipation. The patient should be warned against the dangers of straining at stool. Reactivation of massive hemorrhage associated with hiatus hernia has been observed to result from prolonged straining at stool.

Intubation.—As a routine procedure the intubation of patients with massive hemorrhage into the upper gastrointestinal tract is to be discouraged. This is especially true if the exact location of the hemorrhage

is in doubt The ill-advised passage of any sort of a tube can lead to further damage of a diseased mucosa, disturbance of a poorly organized clot, and even to perforation should there be considerable necrosis associated with the bleeding lesion In patients who are known to be bleeding from a duodenal ulcer and who have persistent nausea and vomiting, intubation of the stomach is a reasonably safe procedure and may permit removal of irritating blood and secretion and thereby relieve the distressing symptoms Continuous but mild suction may be applied until the nausea disappears The tube may then be temporarily clamped off and the patient permitted to take fluids by mouth Should vomiting return, suction can be resumed

There is considerable difference of opinion with regard to intubation of patients whose bleeding may be arising from a gastric or esophageal lesion There is some indication that a decompressed stomach may provide a better environment for gastric bleeding to stop than a stomach in a state of vigorous motor activity due to the presence of a large quantity of partially clotted blood In a small number of patients with uncontrolled bleeding from suspected esophageal varices, Dr Edward W: Bixby, Jr had passed a double or triple lumen soft rubber tube with two separately inflatable rubber balloons attached When the tip of the tube was judged to have passed well into the body of the stomach, the lower balloon was gently inflated and firmly drawn up against the stomach wall at the entrance of the esophagus The second balloon located in the lower end of the esophagus was then gently inflated The effect of these two inflated balloons was to produce gentle tamponade in the regions commonly the source of bleeding in portal hypertension The third lumen could then be used to lavage the stomach or to administer nourishment His results have been promising and to date unmarred by any serious complications Further trial with this method is warranted

Surgical Interference.—If patients suffering from massive gastrointestinal hemorrhage are routinely admitted to the Medical Service, they should be seen by the Surgical Consultant as soon as practicable after admission At the Pennsylvania Hospital there is general agreement between internist and surgeon with regard to the conditions that must be fulfilled before surgical measures are undertaken A reasonably accurate diagnosis as to the source of the bleeding is required The patient must not be in shock or impending shock A careful estimation of the physiological condition of the bleeding patient with the aid of blood volume determinations is a better index of the surgical risk involved than any rule of thumb based upon an estimate of the number of hours elapsing since the onset of bleeding We believe that the restoration of physiologic equilibrium is essential before major surgery is attempted and subscribe to the view recently expressed by Amendola[15] who has stated "With massive blood transfusions and modern anesthesia, a patient who cannot be safely conditioned for major gastric surgery should not be subjected to the added risk of operation "

SUMMARY

1 A prearranged plan is of distinct value in meeting the medical emergency presented by massive gastrointestinal hemorrhage

2 A careful history, physical examination and laboratory study are the cornerstones of successful management of massive hemorrhage

3 Of particular value is the determination of the circulating blood and plasma volume in patients suffering massive hemorrhage It is useful, not only in providing a prodromal sign of impending shock but also in estimating the amount of blood needed to prevent shock from developing

4 Massive, continuous transfusion of whole blood is the method of choice in the treatment of the acute phases of hemorrhage into the gastrointestinal tract

5 The added risk of surgical intervention should not be imposed unless the site of the bleeding is known with reasonable accuracy and there are no evidences of shock or impending shock

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HEADACHE AS AN EMERGENCY COMPLAINT

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Headache is seldom an emergency symptom as judged by life and death standards but the pain is frequently sufficiently severe to assume emergency proportions, at least in the mind of the patient Many headaches which are not appreciably alleviated by the use of analgesics are amenable to treatment with specific medications Effective therapy therefore requires that a specific diagnosis be made in each instance of severe headache

The common causes of severe headache are

1 Migraine
2 Histamine headache
3 Acute infections
   (a) Meningitis
   (b) Typhoid fever
   (c) Infectious mononucleosis
   (d) Rickettsial diseases
   (e) Malaria
   (f) Acute sinusitis and otitis media
4 Cerebral vascular accidents
5 Sinus thrombosis
6 Neuralgia
   (a) Supraorbital
   (b) Sphenopalatine
   (c) Trigeminal
7 Hypertension
8 Sunstroke
9 Trauma
10 "Spinal puncture" headache
11 Menopausal headache

The patient suffering from severe headache is usually concerned primarily with securing symptomatic relief and may be in no mood for a complete history and physical examination It is essential for successful therapy, however, that the nature of the headache be determined in order to avoid the abuse of opiates, delays in diagnosis of underlying conditions, and toxic effects of medications which may be contraindicated In order to accomplish this purpose with a minimum of history taking the following questions will generally suffice

1 Where is the pain?
2 Is this headache unusual or has it been a recurring complaint?
3 History of hypertension, nocturia, albuminuria
4 History of trauma

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TABLE 1

DIAGNOSIS OF HEADACHE BY HISTORY

	Location	Recurrence	Hypertensive Symptoms	Trauma	Fever, Malaise, Chills	Pre-existing Chronic Disease	Mode of Onset	Prodrome	Family History
Migraine	Temporal ocular, occipital	Cyclic interval more or less constant	0	0	0	0	Gradual, daytime	Scotomas, Hunger	+
Histamine	Temporal, ocular, occipital, facial	Occurs in "spells," with free interval between	0	0	0	0	Sudden, day or night	0	Allergy ±
Infectious	Frontal	0	0	0	+	0	Gradual	Fever, chills	0
Cerebral Vascular Accidents	Variable	0	+	0	±	Hypertension plus arteriosclerosis	Gradual—thrombosis, sudden hemorrhage	"Dizziness," confusion, weakness	±
Sinus Thrombosis	Generalized or over involved sinus	0	0	0	+	Mastoiditis, sinusitis, furunculosis	Gradual	Local infection about head	0
Neuralgia	Over involved nerves	Frequent, irregular, unpredictable	0	Minor irritation of "trigger area"	0	Sometimes related	Sudden, severe	0	0
Hypertension	Vertical, occipital	Once started tends to be nearly daily	Visual change, dyspnea, nocturia, edema	0	0	Renal? Idiopathic?	Gradual on waking or with excitement	0	±
Sunstroke	Frontal or generalized	May have a permanent susceptibility as a residuum	0	Exposure to heat or sun	May be extreme	Irrelevant	Sudden	Dizziness, weakness, palpitation	0
Trauma	Anywhere—frontal is frequent	Yes, irregular	0	+	Weakness +, malaise ±	Psychoneurotic symptoms?	Irregular	0	0
Spinal Puncture	Generalized	May recur for 7-15 days	0	Spinal tap	0	0	May be intermittent	0	0
Menopausal	Suboccipital, temporal, vertical	Yes, irregular	0	0	"Hot flashes" frequently accompany	Menopause—natural or surgical	Sudden or gradual, frequent on awakening	0	0

5 Symptoms of systemic infection such as fever, chills, malaises, etc ?
6 History of any pre-existing chronic disease
7 Mode of onset and prodromal symptoms
8 Family history of headache

A reasonably complete physical examination can be done in a few minutes without excessively disturbing the patient Special attention should be paid to the following features

1 General habitus
2 Temperature, pulse, and respirations
3 Level of consciousness
4 Pupillary responses
5 Extraocular movements and nystagmus
6 Ocular fundi
7 Tympanic membranes
8 Tenderness of the paranasal sinuses
9 Odor of the breath
10 Color of mucous membranes
11 Speech defects
12 Nuchal rigidity
13 Blood pressure
14 Enlargement of liver or spleen
15 Cardiac rhythm
16 Motor power of the extremities
17 Reflexes
(a) Tendon reflexes
(b) Special reflexes (Hoffman and Babinski)
18 Jaundice
19 Petechiae

A consideration of each of the common causes of severe headache in the light of the above data will usually lead to a specific diagnosis

MIGRAINE

The pain of migraine headache is characteristically located in the temporal, supraorbital and retrobulbar regions with extension, in bizarre cases, into the back of the neck, the vertex and the forehead True migraine is almost always unilateral, at least at the onset, but radiation across the midline frequently occurs as the pain reaches a climax It is a recurring complaint with intervals varying from a few days to several months in different patients The interval in the same patient tends to be relatively constant Known precipitating factors may exist such as nervous excitement, ingestion of alcohol, or, rarely, use of a known allergenic substance in the diet There is no history of hypertension (in fact most patients with migraine tend to exhibit low blood pressure), trauma, systemic infection, or chronic disease One or more relatives, in most cases, are similarly afflicted The migrainous constitution[1] is frequently disclosed in childhood by episodes of motion sickness, cyclic vomiting, or "bilious attacks"

The headache itself commonly begins on first awakening in the morning It may occur at any time of the day or night, however If the patient is awake during the prodromal period she will notice definite warnings that the headache is imminent These may take many forms Some patients will notice a day of unusual vigor during the preceding twelve hours Nocturnal hunger is a frequent warning Bizarre neurological incidents may herald the approach of trouble—scotomas, blindness, sensory disturbances, and even paralysis These are of such a character that they can readily be interpreted as circulatory deficiency in localized areas of

TABLE 2

DIAGNOSIS OF HEADACHE BY PHYSICAL EXAMINATION

	General Habitus	Temperature, Pulse Respirations	Level of Consciousness	Pupillary Responses	Extraocular Movements, Nystagmus	Ocular Fundi	Tympanic Membranes	Tenderness of Paranasal Sinuses	Odor of Breath	Color of Mucosae
Migraine	Small, slightly built, delicate	Normal	Very slight confusion may be present	Normal (?dilated)	Normal	Normal	Normal	Frontal ±	0	Conjunctivae pale
Histamine	Not characteristic	Pulse rapid	Normal	Normal	Normal (eye flushed on affected side ±)	Normal	Normal	Maxillary and frontal ±	0	Conjunctivae reddened
Infectious	0	Fever, pulse slow or rapid	Varies—usually normal	Normal	Normal except in basilar meningitis	Normal	Inflamed in otitis media or mastoiditis	Marked in acute sinusitis	0	Normal
Cerebral Vascular Accidents	Plethoric ±	Fever ±, tachycardia, Cheyne-Stokes ±	Usually markedly impaired	May be impaired	May be impaired Nystagmus ±	Hypertensive changes changes ±	Normal	0	Uremic?	Plethoric
Sinus Thrombosis	0	Fever, pulse rapid	Delirium ±, drowsy	Asymmetrical in cavernous sinus thrombosis	Marked impairment in cavernous sinus thrombosis	Venous distention, papilledema	Normal	Frontal in cavernous sinus thrombosis	0	Normal
Neuralgia	0	Normal	Normal	Normal	Normal	Normal	Normal	Maxillary, sometimes frontal	0	Normal
Hypertension	Plethoric ±	Pulse may be rapid	Normal	Normal	Normal	Hypertensive changes	Normal	0	Uremic?	Plethora
Sunstroke	0	High fever, tachycardia, tachypnea	Coma is frequent	Dilated	Nystagmus ±	Veins may be full	Normal	0	0	Flushed
Trauma	0	Pulse slow in increased intracranial pressure	Convulsions (epileptiform), coma	Asymmetrical in some cases	Varies	Papilledema (inconstant)	Normal	0	0	Normal
Spinal Puncture	0	Normal	Normal	Normal	Normal	Normal	Normal	0	0	Normal
Menopausal	Age—tense facies	Normal	Normal	Normal	Normal	Normal	Normal	0	0	Normal

	Speech Defects	Nuchal Rigidity	Blood Pressure	Hepatomegaly Splenomegaly	Cardiac Rhythm	Motor Power	Reflexes	Jaundice	Petechiae
Migraine	Slight, transient	Some tenseness of neck muscles is common	Low	0	Normal	Monoplegia may occur rarely	Normal	0	0
Histamine	0	0	Normal	0	Normal	Normal	Normal	0	0
Infectious	0	Marked in meningitis	Normal	Marked in rickettsial inf mononucleosis hepatitis typhoid etc.	Normal	Normal	Normal	±	±
Cerebral Vascular Accidents.	Vary from none to complete aphasia	Marked in subarachnoid or intraventricular	Rises at first. May be normal later	±	Irregular early Normal later	Varies, hemiplegia common	Variable, absent early abnormal later	0	Embolic ±
Sinus Thrombosis	0	±	Normal	0	Normal	Normal	Normal	0	Present in general sepsis
Neuralgia	0	0	Normal	0	Normal	Normal	Normal	0	0
Hypertension	0	0	High	0	Varies	Normal unless residual from old c.v.a.	Normal	0	Occasionally seen
Sunstroke	Not characteristic	0	Low	0	May be slow or rapid	Normal	Vary	0	0
Trauma	Vary	0	Normal	0	Normal	Varies	Vary	0	0
Spinal Puncture	0	0	Normal to low	0	Normal	Normal	Normal	0	0
Menopausal	0	0	Normal	0	Normal	Normal	Normal	0	0

the brain The pain begins gradually and develops to its climax in a period of hours, unlike some of the other vascular headaches It is pounding in character and becomes very severe Vascular changes such as sweating or redness of the face do not occur The superficial temporal artery on the affected side frequently becomes prominent and pressure over it may afford some temporary relief

True migraine occurs almost exclusively in women The physical examination characteristically reveals a small, asthenic, delicately built woman lying in bed with both eyes closed She is turned away from any light source in the room The positive physical findings are limited to this characteristic body habitus, the prominent temporal artery on the affected side, and, in some cases, moderate ptosis of the eyelid of the painful eye The fact that all the other signs mentioned in the preceding list are negative is, however, equally important in establishing the diagnosis

Treatment.—Having established the diagnosis of migraine, specific therapy with vasocontricting substances should be undertaken promptly Opiates should be avoided, not only because of the possibility of habit formation in this recurring difficulty, but also because they are not very effective in relieving the pain The most consistently successful drug for the treatment of migraine headaches is *ergotamine tartrate* * Although it produces more unpleasant side-effects than any of the other practical medications for this purpose it is most likely to give relief from pain It should be administered subcutaneously or intramuscularly in a dose of not less than 0 25 mg or greater than 0 50 mg The intravenous use of ergotamine tartrate in the treatment of migraine has nothing to recommend it If relief of pain has not begun within one-half hour the dose may be repeated Not more than 1 mg should be given in any one twenty-four hour period If the headache has not been in progress over four hours this treatment will almost always be followed by relief within one hour Side effects of nausea and vomiting are common.

If the headache recurs frequently enough to become a major problem, other hypodermic and oral medications should be tried in an effort to discover the ideal program for the particular patient in question It is impossible to predict, with any certainty, which of the following will be most helpful without actually testing them on subsequent occasions of pain

Oral Preparations—1 Cafergone † Of all the oral medicaments which we have had an opportunity to study, this has proved the most successful The patient is instructed to take two tablets at the very beginning or during the prodrome of a headache If complete relief is not achieved in one hour the dose is repeated Nausea and vomiting are occasionally produced but the incidence is much lower than with ergotamine tartrate hypodermically If the headache for which this is taken

* Gynergen (Sandoz) (1 cc contains 0 50 mg)

† Each tablet contains ergotamine tartrate (Gynergen, Sandoz) 1 mg and caffeine citrate 100 mg

is not relieved by it, an injection of Gynergen may be given without fear of cumulative or additive effect

2 Octin,* though very helpful by hypodermic injection as described below, is seldom useful by mouth However, its freedom from unpleasant side effects and its safety make it worth trying on all patients with migraine, even though the percentage of patients who derive relief from their headaches from the oral use of this drug is small It is our custom to give one tablet containing 130 mg (2 grains) of Octin Mucate with 650 mg (10 grains) of acetylsalicylic acid and 500 mg of bromisovalum† by mouth If relief has not been obtained in one hour the dose must *not* be repeated Instead, one of the hypodermic preparations should be used

Hypodermic Preparations—1 Dihydroergotamine,‡ given by hypodermic injection in doses of 1 mg, is less frequently successful than ergotamine tartrate but it also produces fewer unpleasant side effects However, there are a considerable number of migraine sufferers who derive prompt relief from moderate doses of this material It is our custom, when "standardizing" a new patient, to administer 1 mg (1 cc) of the solution subcutaneously or intramuscularly at the onset of pain This is repeated in one hour if complete relief is not obtained with the first dose If the result is satisfactory the material can be used on subsequent occasions without risk of a tolerance developing and with no practical risk of ergotism Generally speaking, it is considered unwise to give any ergot preparation more often than three times weekly Patients with obliterative arterial disease, either due to arteriosclerosis or endarteritis, are poor subjects for the use of any ergot derivative although major tragedies are seldom reported, even in this group We have [illegible] one patient who, against medical advice and in spite of many [illegible] prevent it, has taken 0.5 mg of ergotamine tartrate by injection [illegible] day for the past four years So far he shows only some [illegible] the caliber of the retinal vessels as evidence of the toxic effects of the drug No similar long term observations have been made [illegible] stant use of Dihydroergotamine but one would expect the [illegible] dangerous effects to be less than with ergotamine tartrate [illegible] with migraine cease to have their headaches early [illegible] nevertheless, one should be cautioned not to give [illegible] for headache developing during gestation

2 Octin, in the form of the hydrochloride [illegible] injection has proved very useful in controlling [illegible] some patients Its main pharmacologic [illegible] vasoconstricting, smooth muscle relaxing [illegible] combination of effects for a drug to be used [illegible] Thus this drug can be used with [illegible] increase dysmenorrhea when given [illegible] headaches so frequently occur) and [illegible]

* Methyl iso-octenylamine (F [illegible]
† Bromural (Bilhuber Knoll)
‡ D H E 45 (Sandoz)

ing The only untoward effect of which we are aware is a tendency to produce transient hypertension in some patients This has never led to serious complications in our experience but, nonetheless, we never administer this material to any patient suffering from hypertension or organic heart disease Before it is declared "safe" for any patient several test administrations should be performed under close medical supervision It is our custom to give 50 mg intramuscularly with the patient recumbent The blood pressure is then taken every ten minutes If there is no rise in blood pressure within twenty minutes a second dose of 50 mg is given and the blood pressure determinations are continued If there is still no increase (or less than 20 mm of mercury systolic and 10 mm diastolic) the patient is instructed to give herself 75 mg as an initial injection at the onset of headache If relief is not complete within one hour she may take 25 mg at that time If a moderate rise of blood pressure (20 to 30 mm systolic and 10 to 20 mm diastolic) ensues no second test dose is given and the patient is instructed to use 50 mg as her therapeutic dose If greater rises in blood pressure occur we deem it unwise to use this material in that particular patient Moderate to marked elevations of blood pressure occur in only about 30 per cent of patients to whom Octin is given in these doses

In our experience about 50 per cent of patients suffering from migraine can derive good relief by this technic Tolerance to the drug does not develop and there are no cumulative effects known One of our patients has now been given over 300 injections of 50 to 150 mg each over a period of three and one half years with no apparent toxic effect and with a continuation of its original beneficial effect If the same area is used for injections too frequently some fibrosis will develop in that region Patients receiving this material should remain recumbent for one hour after the injection

3 Octin-Dihydroergotamine mixtures have proved beneficial to a rather large group which derives no benefit from the Dihydroergotamine alone and who develop excessive hypertension with full doses (100 mg) of the Octin Frequently these patients will be relieved by a single injection of a mixture of 50 mg of Octin and 1 mg of Dihydroergotamine The ability of the Octin to relax smooth muscle helps to prevent the vomiting which occasionally follows the use of ergot We have not had occasion to see patients with migraine during pregnancy who could not be relieved by the Octin alone However, in such a case if the pain were unbearable the danger of inducing abortion with this mixture should be considerably less than with ergot alone

Nicotinic acid, antihistaminics, vitamin therapy, oxygen inhalations, epinephrine, trichlorethylene, and ascorbic acid—all recommended from time to time for this condition—have not, in our hands, proved sufficiently useful to be worth trying They are sometimes helpful in other types of headaches but true migraine is refractory to all of them

Subsequently, if the headaches continue to be a frequent and disabling symptom, an attempt to increase the patient's "tolerance" to

histamine as suggested by Butler and Thomas[3] is worthwhile Several minor modifications of their original technic have been helpful We use 10 per cent glucose in normal saline solution as the diluent for the histamine because of the well known tendency of these patients to develop hypoglycemia under stress Likewise we dilute the 1 mg of histamine base (2 75 mg of histamine acid phosphate) with 1000 cc of solution instead of 500 cc , since we can more accurately adjust the rate of flow in that manner We administer the "drip" once daily for fifteen days and the patient is instructed to give to herself, after discharge from the hospital, 0 1 cc of a 1 20 dilution of histamine acid phosphate subcutaneously each day We do not recommend gradually increasing the dose of these subcutaneous injections They may gradually be reduced in frequency and finally, after several months, discontinued

We have been unable to predict which patient is likely to derive benefit from this course of treatment and which is not Certainly their response to a test dose of histamine given subcutaneously does not give pertinent information in this regard Suffice it to say that satisfactory results occur with sufficient frequency (40 to 80 per cent) to make it worthwhile in treating any patient with migraine or histamine headache (see below) of sufficient severity and frequency to be considered a major disability

HISTAMINE HEADACHE

In general the histamine headache greatly resembles migraine in its location, intensity and character However, there are a few guideposts which we use as differential criteria The secondary vascular phenomena are much more prominent in this type of attack The face may be flushed on one side, the eye distinctly inflamed, and superficial tenderness may be present The family history is less definite The onset of pain is much more abrupt, frequently reaching maximum intensity in a few minutes whereas migraine usually develops over a period of hours The history of motion sickness in childhood, of bilious spells and cyclic vomiting is not as characteristic as it is in migraine Histamine headache is common in males The headaches tend to occur in "spells," with frequent distress over a period of weeks or months followed by a long period of complete freedom from attacks The histamine headache wakens the patient frequently from a sound sleep whereas migraine tends to develop gradually after the patient awakes spontaneously A definite relation to some allergenic substance—almost always food—can usually be established

Treatment.—Since the pain itself is produced by intracranial vasodilatation in the same way as migraine, the same therapy is effective in relieving the pain It is our impression, however, that Ergin is effective in histamine headache even more frequently than in migraine Long range treatment should be aimed at, avoiding specific allergens by a strict elimination diet Half hearted attempts to avoid trouble by eliminating single foods are not likely to meet with success One must start with practically a starvation regimen (we use a diet limited to lamb, rice

and maple sugar) for one week New foods are then added one at a time until symptoms are reproduced The offending food is then "banned" and the program continued until all allergenic foods are isolated If this program also meets with failure and the symptoms are sufficiently severe and frequent to justify it, an attempt to increase the patient's tolerance to histamine should be undertaken in these patients also, as described under migraine (above) We have seen no patient whose headaches, either migraine or histamine headache, could be prevented or relieved by the use of "antihistaminic substances"

HEADACHE OF ACUTE INFECTIONS

The headache of acute infections may be extremely severe This is true particularly of meningitis and the rickettsial diseases It is generally an isolated incident in the patient's experience and is described as a dull, aching, throbbing pain usually frontal in location In meningitis the pain moves to the cervical region as the local involvement of the meninges becomes more marked In sinusitis and otitis media the pain will center over the involved area The differential diagnosis of headache due to infection is usually easy when the history of fever, malaise and chills is obtained and when none of the constitutional, prodromal or characteristic features of other headaches are present The presence of rash, jaundice, splenomegaly or generalized lymphadenopathy will aid in determining the specific etiology of the underlying illness

Treatment.—The treatment for these headaches is, of course, the therapy for the underlying illness In addition, however, the salicylates, fortified if necessary with codeine, will usually promptly control the pain One must not be lulled into complacence by the relief of pain which follows these medications when a bulging ear drum needs incision

HEADACHE DUE TO CEREBRAL VASCULAR ACCIDENTS

In cases of intracerebral hemorrhage, thrombosis or embolism the pain is usually referred to the surface of the skull overlying the involved area Hemorrhage from the internal carotid artery at or near the circle of Willis produces a sudden sharp pain over the temple Subarachnoid hemorrhage is accompanied by a sudden severe pain over the back of the neck and in the suboccipital region These pains all come on suddenly in cases of hemorrhage, whereas the discomfort accompanying thrombosis may begin gradually and build up slowly It is essential that the pain of vascular accident be differentiated from the hypertensive headaches from which these patients may have been suffering in the past Frequently the headache precedes unconsciousness by such a short interval that no one will be made aware of its existence

Physical examination usually reveals some impairment of consciousness The body temperature may be slightly elevated The pulse may be slow or rapid or normal depending on the location and extent of the damage and secondary changes in intracranial pressure Cheyne-Stokes

respiration is a common phenomenon in all types of cerebral accidents The pupils are frequently unequal and the extraocular movements may be impaired Nystagmus may be present There may be slurring of speech or complete aphasia Nuchal rigidity is characteristic of subarachnoid hemorrhage or an intracerebral hemorrhage which has extended into the subarachnoid or intraventricular spaces

Within the first few hours after a vascular accident to the brain (particularly in cases of hemorrhage) the cardiac rhythm may be severely altered At first the pulse may become slow with periods of ventricular escape, ventricular premature contractions, and increasing pulse pressure Later, as the effects of vagal stimulation wear off, tachycardia and narrowing pulse pressure will supervene Patients suffering from chronic auricular fibrillation may suffer a cerebral embolus from disintegration of an intra auricular thrombus The motor power of the extremities will be severely impaired Early in the incident there will be a period of "spinal shock" with complete paralysis or weakness of all limbs With the passage of time, however, the paralysis resolves into a typical pattern dependent upon the location of the lesion Initially there will be areflexia, later the pathological reflexes described by Babinski and Hoffman will develop Progressively increasing pyrexia associated with hemorrhage within the brain is characteristic

Treatment.—Treatment for the headache is not usually a problem since unconsciousness develops so promptly in most cases as to make the pain an inconsequential matter However, particularly in patients with cerebral embolism, the pain may be persistent and annoying and the level of consciousness may remain sufficiently high to require therapy for the discomfort Opiates should be avoided because of their depressant effect on respiration Salicylates and caffeine are useful If unsuccessful Demerol, in small doses (50 mg hypodermically), is permissible

HEADACHE OF SINUS THROMBOSIS

The modern use of antibacterial preparations has fortunately made this a rare occurrence. However, it should be kept in mind whenever severe, constant, throbbing headache made worse by coughing or straining occurs in the course of a suppurative infection about the head The condition is characterized by a septic thrombosis of the cavernous sinus Paralysis of the third, fourth and sixth cranial nerves may develop Proptosis is common and periorbital edema may be marked

Treatment should be directed at the underlying condition There is no contraindication to the liberal use of salicylates, codeine and Demerol to control the pain

NEURALGIAS OF THE FACE AND HEAD

The pain of neuralgias about the face and head is characteristically very severe sudden in onset not varied by changes in intracranial pressure (coughing, sneezing etc), and located over the area of distribution

of the involved nerve Secondary muscle tension may produce additional discomfort in the head and neck as a complicating factor—a "tension headache" superimposed on a neuralgia The neuralgic pains are likely to be a recurring complaint The pain builds up to its maximum intensity within a few seconds or minutes of its onset It usually occurs after some mechanical irritation to a "trigger zone"

The distribution of the supraorbital branch of the fifth nerve may cause confusion between neuralgia involving it and true migraine A simple diagnostic as well as therapeutic test can be performed by infiltrating the subcutaneous tissues of the forehead, just above the supraorbital notch, with 1 or 2 cc of 1 per cent procaine solution This will promptly relieve the pain of supraorbital neuralgia but will not affect the discomfort of other types of headache involving this region

Treatment.—All types of neuralgia can be relieved by adequate doses of opiates and, if the attacks occur at rare intervals, there is no contraindication to their liberal use However, if the pain recurs frequently or over a long period of time the dangers of addiction are great and opiates should be discarded in favor of more permanent therapy such as surgical resection Cocainization of the sphenopalatine ganglion within the nasal cavity usually gives effective relief from neuralgia of this particular nerve The use of large amounts of thiamine hydrochloride by injection (50 mg daily) has been followed in a considerable number of cases by complete relief of symptoms and should be tried before more radical surgical measures are undertaken

HYPERTENSIVE HEADACHE

The hypertensive headache may occasionally be severe and, occurring as it does in a patient of labile emotional responses, will require prompt attention The pain may be generalized but as emotional tension becomes a more and more important adjunct the pain extends into the back of the neck The hypertensive headache is frequently present on waking in the morning as a dull, nagging discomfort across the frontal region and behind the eyes Symptoms of hypertensive cardiovascular-renal disease such as nocturia, dyspnea, failing vision and the like will frequently be admitted Physical examination will show a florid complexion, hypertension, varying degrees of vascular change in the retina, frequently papilledema, and cardiac enlargement

Treatment.—The safest symptomatic treatment for a single attack of severe hypertensive headache is a combination of acetylsalicylic acid 650 mg (10 grains) and codeine 32 mg ($\frac{1}{2}$ grain) with one of the short-acting barbiturates such as Seconal, 50 to 100 mg ($\frac{3}{4}$ to $1\frac{1}{2}$ grains) Ergotamine tartrate usually is effective in relieving the pain but should, I believe, be used with considerable caution in view of its vasoconstricting effect Tablets containing 1 mg of ergotamine tartrate and 100 mg of caffeine citrate are sometimes useful and, if used only occasionally, are probably safe for this purpose One or two of these tablets will usually suffice and are well tolerated

Octin should be scrupulously avoided in the patient with hypertension

Subsequent control of the headaches will require control of the hypertension In this regard it may be noted that many patients on whom lumbar sympathectomy has been performed for hypertension will remain free of headache postoperatively even though the blood pressure has not been greatly affected The same may be said for the use of potassium thiocyanate It should be reemphasized that potassium thiocyanate should not be used in the treatment of hypertension if significant renal impairment has occurred Hypertensive patients with mild headache on awakening in the morning frequently obtain considerable relief by sleeping with the head elevated on several pillows

HEADACHE ACCOMPANYING SUNSTROKE

The headache which accompanies the phenomenon of "sunstroke" may be very severe It usually involves the entire head in a throbbing pain There is a definite history of exposure to direct sunlight over a long period of time (several hours) The syndrome may be ushered in with a shaking chill, followed by headache and high fever (105° F is not uncommon) Physical examination shows fever, tachycardia, rapid respirations, moderate to severe impairment of consciousness, hypotension, and flushing of the skin There may be minor disturbances of cardiac rhythm

Treatment.—Treatment of the headache, as well as the general condition, requires prompt reduction in the body temperature This can be accomplished by immersion in cool or cold water up to the neck The use of cold saline solution intravenously and of cold enemas may be wise in extreme cases Salicylates and codeine are helpful both as analgesics and as antipyretics

TRAUMATIC HEADACHE

Though many mild headaches occur after traumatic incidents of minor or major severity, the pain seldom becomes of such intensity as to require emergency treatment except in the case of subdural hematoma This complication may arise at any time from a few hours to several months after a blow to the head The blow need not be a severe one, although those which are sufficiently forceful to cause transient loss of consciousness are more likely to be followed by this complication Typically, the patient recovers from the immediate effects of the blow only to develop later, after a "lucid interval" of varying length, a constant dull but severe headache which gradually increases in intensity The consciousness becomes dulled and memory clouded so that the original blow may not even be recalled The pain is frequently, but not always over the site of the lesion Vomiting of projectile nature will occur if the intracranial pressure is greatly increased

Physical examination will usually reveal distention of the retinal veins

and varying degrees of papilledema if the lesion is large Neurological signs will depend upon location of the hematoma Spinal puncture discloses elevation of pressure and, in some cases, xanthochromic or bloody spinal fluid. Experienced examiners claim to be able to detect dullness to percussion over the lesion A pneumoencephalogram may be required to localize the lesion preparatory to surgical exploration It must be remembered, however, that in these cases as in any other with increased intracranial pressure, spinal puncture should be performed with caution because of the risk of herniation of the cerebellum and medulla into the foramen magnum as the pressure is suddenly lowered We make it a rule always to have a syringe containing 10 cc of sterile saline solution on the tray when such a puncture is performed Injection of this solution through the spinal needle has been effective in at least one case where respirations ceased during a spinal puncture

Treatment.—The pain itself is refractory to all analgesics and requires evacuation of the clot by surgical means for its correction If surgical facilities are not immediately available, the intravenous injection of hypertonic solutions (50 cc of 50 per cent glucose) may give transient relief by reducing the intracranial pressure

"SPINAL PUNCTURE HEADACHE"

The headache which frequently follows spinal anesthesia or diagnostic spinal taps is not commonly regarded as an emergency except by those who have experienced it The headache involves the entire head in a sensation of severe pressure It does not occur commonly in patients who have been allowed to be up and about immediately after the spinal tap but is common in those patients who, according to common practice, are kept flat in bed for several hours

Treatment.—Once the pain has developed variation in position is not likely to be helpful Acetylsalicylic acid 650 mg (10 grains) and phenobarbital 65 mg (1 grain) are standard treatment but we have recently had some success in giving Octin by mouth to these patients The initial dose should be 130 mg (2 grains) and this may be repeated in one hour It can be effectively given in combination with the aspirin and phenobarbital If this proves ineffective adequate doses of codeine—32 to 65 mg ($\frac{1}{2}$ to 1 grain)—are permissible

MENOPAUSAL HEADACHE

A few women, following natural or surgical cessation of the menses, develop an intermittent paroxysmal headache of great severity which is, in respect to location and character of the pain, practically indistinguishable from true migraine. In fact, women who have suffered from true migraine all their lives may enjoy a few months of freedom from pain after the menopause only to have the headaches return after this short space of relief The important feature of the history is the fact that the headaches have not been present before the menopause or, if migraine

had been present in youth, there was an interval of relative freedom before they returned in full force This headache seldom demonstrates the spectacular prodromata of migraine such as scotomas It is frequently accompanied by nausea and vomiting The pain is more frequently cervical and suboccipital but it may be temporal in location

Treatment.—Menopausal headache can usually be relieved by the same medications which are helpful to the true migraine sufferer However, after the first headache has been relieved, subsequent attacks can almost universally be prevented by the administration of appropriate amounts of estrogenic substances by mouth Parenteral injections are in no way superior to oral medication in this regard It is our custom to start with 1 25 mg of natural conjugated estrogenic substance daily for a period of one month The amount is then gradually reduced at three or four week intervals until its use can be discontinued The usual precautions should be observed, i e the material should not be given in the presence of a strong family history of cancer or the existence of known

TABLE 3

SUMMARY OF TREATMENT OF HEADACHE

	Symptomatic Relief	Long Range Program
Migraine	Cafergone tablets. Octin ‡ No opiate Dihydroergotamine † Cold compresses Dark room.	Histamine desensitization Psychotherapy—Thyroid (in selected cases)
Histamine	As above. Octin‡ is frequently effective No opiate	Elimination of specific allergens. Histamine "desensitization."
Infectious	Analgesics.	Treat underlying infection with specific drugs.
Cerebral Vascular Accidents	Hypertonic glucose Caffeine Analgesics with caution	General measures. The headache usually does not persist.
Sinus Thrombosis	Analgesics in full doses Cool compresses	Specific antibacterial therapy
Neuralgia	Analgesics in full doses	Thiamine hydrochloride 50 mg. I.M daily Vitamin B complex by mouth. Remove infectious foci. Surgical resection of involved nerve.
Hypertension	Cafergone (2 tablets only with caution) Salicylates and barbiturates Rest.	Sympathectomy may relieve intractable headache even in cases where it does not "cure" hypertension.
Sunstroke	Immediate reduction of body temperature with cold baths cold enemata even cold I V drip in critical cases Cardiac support	Avoid exposure to heat and/or sun
Trauma	Surgical exploration if indicated by focal signs or marked increase in intracranial pressure Do not x-ray Make diagnosis clinically No opiate Hypertonic glucose (50 cc. of 50% I V) may help.	Nonspecific. Mild analgesics and/or physiotherapy
Spinal Puncture	Aceto salicylic acid 0.0 mg. Bromural§ 500 mg. Octin‡ 130 mg. by mouth Codeine if necessary	

Each tablet contains ergotamine tartrate 1.0 mg and caffeine citrate 100 mg —Sandoz
† D H E 45 (Sandoz)
‡ Methyl iso-octylamine (Bilhuber Knoll)
§ Bromovalum (Bilhuber Knoll)

cancer or precancerous lesions in the patient. However, we have found it occasionally necessary to give the material even in the face of these theoretical contraindications in patients whose suffering is so great that the possibility of suicide seemed greater than the dangers of carcinogenesis If the diagnosis is correct and the therapy adequate, the headaches will cease at once. If, on this program, the headaches continue some other cause for them should be sought

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THE MANAGEMENT OF SEVERE INTRACTABLE ASTHMA (STATUS ASTHMATICUS)

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Status asthmaticus is the name most commonly applied to that condition of severe continuous asthma that persists despite the use of the usually effective medications It occurs most frequently in the chronic asthmatic patient whose symptoms generally are relieved by the usually effective remedies as epinephrine, ephedrine and aminophylline With the failure of these remedies, the mental anguish of the patient is added to the severe physical difficulty

In this type of asthma, the bronchi and the bronchioles become obstructed by a thick, viscid exudate in addition to the bronchial muscle spasm and mucosal edema All these factors tend to trap air in the lungs and expiratory dyspnea increases Cyanosis appears with the development of anoxia and is in proportion to the oxygen deficiency in the blood The patient becomes extremely ill, the pulse becomes rapid and weak, fever may occur, and there is often an unproductive cough The breathing becomes rapid and shallow, the patient gradually becomes comatose, and death is imminent

Physical examination reveals musical rales throughout the chest, typical of bronchial asthma As the condition progresses areas of absent or diminished breath sounds are found, with the development of obstructive emphysema Eosinophils which are present in the sputum early in the attacks generally give way to leukocytes [1] The blood pressure may become elevated and albuminuria may be present Death, when it occurs, may be due to asphyxiation, cardiac failure, or if untreated, to exhaustion and dehydration

Status asthmaticus must be considered a medical emergency, and treatment should first be directed to restoring adequate ventilation of the lungs If possible, the patient should be *hospitalized* Not only can more competent treatment be carried out in the hospital, but also the change of residence may remove the patient from contact with the exciting cause or causes of his continued asthma No specific allergic treatment should be attempted at this time Injection of allergen extracts and bacterial vaccines will often increase the asthma

Once the patient is hospitalized a rational and orderly program of treatment should be followed *Epinephrine* in a 1 1000 aqueous solution should be given in 0 5 to 1 0 cc (7 to 15 minims) doses by hypodermic injection and repeated in one hour If relief is obtained, 0.25 cc (4

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minims) should be given every waking hour Simultaneously epinephrine 1.500 in peanut oil,[2] or if the oil causes severe local reaction, 1 500 in gelatin,[3] may be given at night in 1 cc doses subcutaneously

When no relief is obtained from epinephrine, it is usually due to the presence of mucous plugs in the bronchial tree that have not been dislodged The term, "epinephrine fast," has been applied to this condition The administration of *aminophylline* intravenously in 0 25 to 0 5 gm ($3\frac{3}{4}$–$7\frac{1}{2}$ grains) doses in 10 to 20 cc of normal salt solution may be more effective and may be repeated every six hours The intravenous injection of aminophylline must be given slowly, at the rate of 1 ml per minute to avoid possibility of circulatory collapse This drug may also be given intramuscularly and by rectum in doses of 0 5 gm ($7\frac{1}{2}$ grains) The intramuscular administration of aminophylline is given in 2 cc of normal salt solution, while the rectal administration may be in 10 cc of solution, or by suppository in cocoa butter

Iodides, by stimulating mucous secretions, may help loosen the bronchial plugs Either the sodium or potassium salt in 0 64 gm (10 grains) doses by mouth may be given three times a day concurrently with other medication. Vomiting is very effective in eliminating the loosened mucous plugs, and Cooke[4] has recommended *ipecac* (10 to 15 ml of the syrup) for this purpose Atropine and belladonna are not recommended because of the drying effect on the secretions, making it more difficult to eliminate the bronchial plugs

Oxygen is of great help in relieving the anoxia and may be administered in a tent, or by means of a mask or nasal tube Some patients strongly object to the tent and to masks, which have the psychological effect of limiting breathing space The nasal tube, metal or rubber, should be well lubricated with petrolatum and inserted along the floor of the nostril

A mixture of *helium and oxygen* is recommended by Gay[5] and has the advantage of its greater diffusibility which decreases the degree of respiratory effort Barach[6] has advocated the inhalation of a mixture of 20 per cent helium in oxygen in status asthmaticus He recommends the administration of the mixture by mask three times a day, increasing the percentage of oxygen if the anoxemia is marked A disadvantage is the relative cost of the helium, and 100 per cent oxygen is generally satisfactory

Bronchoscopy is of definite benefit at times in intractable asthma, and may even be a life-saving procedure by aspirating the thick tenacious mucous plugs from the bronchi Waldbott[7] considers it an obligatory procedure in a moribund asthmatic

Measures must be taken to combat the dehydration which develops in all patients with prolonged asthma, and *intravenous fluids* are indicated The slow administration of 5 per cent glucose in 1000 cc of saline, to which has been added 1 gm (15 grains) of aminophylline, is the method of choice at the Pennsylvania Hospital Keeney[8] has proposed the use of 50 cc of a 50 per cent sucrose solution for its dehydrating

effect on the bronchial mucosa In the presence of considerable moist rales it is definitely helpful, but in the dry chest, with few rales and little or no expectoration, it seems that it would aggravate rather than benefit the condition

After the above measures have been put into effect to relieve the critical state of the patient, *sedation* can then be considered Persistent severe asthma causes physical strain on the accessory muscles of respiration, and, with the added mental anguish, sleep is impossible Yet, with exhaustion becoming more pronounced, the need for sleep is apparent

Gay[3] is emphatic in advising against the use of morphine and it is true that many deaths from asthma appear to have been due to the injudicious use of this drug Cook[4] believes it may be given guardedly and in small doses to lessen cough and to allay distress, but not in amounts that would stop cough or slow respiration. Before giving morphine or any strong sedative, we believe some guide may be obtained from a very careful examination of the lungs When even a small area of the chest reveals the absence of asthmatic rales in contradistinction to the loud wheezes in adjacent areas, morphine should never be given When no such area is detected morphine may be given with great care In patients in status asthmaticus who have been given morphine sufficient to slow respiration, we have found *caffeine and sodium benzoate*, 0 5 gm (7½ grains) intramuscularly, to be life saving It may be repeated in four hours We have seen such patients relieved sufficiently for them to relax into a natural sleep for an hour or two after receiving caffeine For mild sedation, the barbiturates such as phenobarbital 0 032 gm (½ grain) t i d , or chloral hydrate 0.32 to 0 64 gm (5 to 10 grains) are helpful Codeine sulfate 0 016 gm (¼ grain) by hypodermic injection is preferred to relieve the stubborn cough For relaxation, a mixture of *ether and olive oil* (2 to 3 ounces of each) instilled into the rectum will give relief for six to eight hours

GENERAL CARE

The general care of a patient with prolonged intractable asthma is of great importance. The diet should be liquid for the first few days of the attack As the dyspnea decreases, more solid food may be added gradually, being careful to avoid any foods to which the patient is known to be sensitive Abdominal distention tends to increase the dyspnea, and great care should be taken to prevent its occurrence Cathartics should be given at the onset of treatment, and an ounce of magnesium sulfate is recommended Proper elimination should be maintained throughout the attack by means of mild laxatives and enemas

In prolonged attacks with persistent anorexia, intravenous administration of amino acids will often bring startling results by combating dehydration and relieving the starved tissues These are best given with 1000 cc of 5 per cent glucose twice daily Any of the commercial preparations of amino acids are satisfactory

Psychotherapy must not be neglected in the treatment of these un

fortunate patients The mental alarm of a patient with intractable asthma is considerable and must be treated The physician and others in attendance should be careful not to reflect the patient's anxiety A confident, hopeful attitude is of great importance to the patient and will go far toward overcoming his own anxious tension We would like to emphasize that the administration of sedatives is not a form of psychotherapy

COMPLICATIONS

Fever as a complication of status asthmaticus is not uncommon. It may be due to bronchial infection or, according to Clarke,[1] due to absorption of long retained exudate in the bronchioles The fever usually subsides promptly with relief of the asthma, but if it persists over twelve to twenty-four hours, penicillin therapy should be instituted It may be given by hypodermic injection, 200,000 to 300,000 units daily, or by inhalation A nebulizer may be conveniently attached to the tubing from the oxygen pressure tank Ten thousand units of penicillin per cubic centimeter nebulizes well One to 2 cc should be inhaled every three hours

Patients with cardiac disease, and the aged, should be watched for evidence of *cardiac failure* Edema of the extremities and enlargement of the liver are the most reliable signs since pulmonary symptoms of failure are obscured by the asthma In the presence of early cardiac failure it is wise to fully digitalize the patient, although the administration of digitalis 0 2 gm (3 grains) three times a day for two days may be sufficient to carry the patient through the asthmatic attack Hypertension in the presence of asthma is no contraindication to the use of epinephrine since the relief of the dyspnea will lower the blood pressure [9]

ILLUSTRATIVE CASE HISTORY

J G , a white man aged 55, was first admitted to the Pennsylvania Hospital in August 1941 for study of recurrent attacks of bronchial asthma He had been remarkably well all his life until he developed a persistent cough eighteen months previously which was diagnosed as chronic bronchitis Since then he had experienced recurrent attacks of difficult breathing and cough with audible wheezing requiring epinephrine for relief Except for frequent "colds," the past history was negative He suspected that his son had hay fever, but there was no other family history of allergy Physical examination was not remarkable, there was no evidence of respiratory infection and the chest was clear at the time of examination Allergic studies and skin tests revealed markedly positive reactions to house dust, dog dander and feathers, and slightly positive reactions to timothy and orchard grass pollens Chest x-ray was essentially negative Laboratory studies were negative save for 7 per cent eosinophilia He had no attacks of asthma during this stay in the hospital On discharge he was referred to the Allergy Clinic, and he did well following elimination of feather pillows and hyposensitization therapy with dust extract

In December 1943 the patient developed an upper respiratory infection fol-

by severe persistent asthma which for the first time did not respond to
ame or aminophylline. After three days he was admitted to the Passaic
Hospital in status asthmaticus. Physical examination revealed lids, ne
ions with middle wheezing. Dullness was imparted over the right middle
posterior and in the axilla, and moist rales were present over these areas.
, numerous wheezing was heard elsewhere throughout the chest. The
was not remarkable. Blood pressure was 170 S. Temperature on admission
F., pulse 120, respiration 28.

by intakes of aminophylline 0.25 gm. by mouth every three minutes
e doses, then 0.25 gm. every hour, supplemented by aminophylline 0.5
gm. by rectum six hour intervals for three doses. The patient was
n subcutaneous for four days because of the pronounced infection. Adre-
phrine stimulant in strength was given, and the patient did not die. He was
ed great relief. For the next three years on this quite well and to
management with only occasional attacks of mild asthma.

ne 1947 the patient again developed a severe and asthma which eventually
more severe, and approached the condition of status asthmaticus with
o response to medication. He was admitted to the hospital with a temper-
1 0F. Physical examination revealed dyspnea with difficulty in
in the inspiratory phase, hyperresonance of the chest, tenderness of 1.6000
ment, and many of the chest revealed signs of a mild pneumonitis.

ed on the treatment consisted of aminophylline 0.2 gm. 5 minims every
aminophylline by suppository and by rectum as needed. Prednisone 20 mg.
ne in divided doses was given over a six day period for the severe
. Symptoms subsided gradually, temperature returned to normal, a
ed and symptoms of 5 no cough. The patient was discharged greatly im-
referred back to the Allergy Clinic.

well for the next two years under continuous allergic management and
0 pounds.

ber 1948 the patient noted gradually increasing asthma, which over
ew period developed into status asthmaticus. Medication failed to give
and he was completely incapacitated. He was admitted to the Passaic
ospital in November. Physical examination revealed a marked increase
dyspnea with hyperresonance throughout the chest. Expiration was prolon-
ble and there was marked inspiratory distress. The heart was normal.
pressure was 142/84, temperature and pulse were normal. Urine and blood
were normal, except for a 0 per cent eosinophilia.

ng on the second day intravenous aminophylline and aminophylline as before
ve aminophylline 1 gm. in 500 cc. of saline was given intravenously
ly nasal endotracheal was necessary to remove the secretions and destroy
s induced emphysema, but the patient did not require complete use of
. He was bronchoscoped on November 19 and again on November 22
l. Bronchoscopy reported a thickened mucous membrane in the larynx and
ondial tree with the presence of a thick tenacious secretion in typical of
in individuals with an allergic background. A considerable amount of
was aspirated from which an autogenous vaccine was later prepared.
l bronchoscopy the patient experienced considerable relief and from
improved rapidly. A second bronchoscopy three days later showed a
on and an improvement in the mucous membrane. A x-ray of the chest
the presence of generalized emphysema of both lung fields with in
bronchovascular markings. The patient was discharged symptom-free
ber 27, 1948. Since that time he has continued to have

attacks of asthma in spite of treatment with dust extract and an autogenous vaccine

Comment.—Status asthmaticus of various stages of severity is presented in the above illustration At the time of the first admission hospitalization alone was probably sufficient to bring relief of symptoms In later admissions it was necessary to resort to more and more therapeutic procedures The presence of secondary infection required the use of antibiotics At the time of final admission, the asthmatic state had become more resistant and was relieved only partially by the usual methods of treatment Bronchoscopy was necessary before complete relief was obtained

The course of this case likewise demonstrates the gradual increase in severity of the asthma which sometimes occurs in spite of careful allergic therapy The decreased response to treatment, together with the development of emphysema and probably other pathological changes, suggest an ultimately poor prognosis

SUMMARY

As a guide to the physician in the treatment of status asthmaticus we are tabulating our recommendations and usual routine

1 Hospitalize patient if possible
2 Epinephrine (1·1000) 1 cc by hypodermic injection followed by 0 25 cc every hour
3 Aminophylline 0 5 gm intravenously in 20 cc of salt solution every six hours, or continuously in 1000 cc of 5 per cent glucose
4 Potassium Iodide 10 grains three times a day
5 100 per cent Oxygen by nasal tube
6 Caffeine and Sodium Benzoate 0 5 gm intramuscularly repeated in four hours
7 Intravenous Fluids
8 Ether and Oil—two ounces of each by rectal tube
9 Sedation Phenobarbital ½ grain three times a day

In this brief discussion we have mentioned many remedies and procedures However, the physician should select those best suited to the immediate needs of the individual patient He should be careful to avoid overmedication It is a common feeling among physicians that the treatment of choice of status asthmaticus is to "throw the book" at the patient, in the hope that one of the medications administered will be helpful We emphasize that it is important to consider the rationale for the use of these medications and procedures, and utilize them as the need presents itself It should also be noted that allergies to drugs do exist, and when they are present, the physician should select some other drug of entirely different chemical properties

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THE DIAGNOSIS AND TREATMENT OF MEDICAL PULMONARY EMERGENCIES

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The pulmonary emergencies that are encountered in the practice of medicine include pulmonary hemorrhage, spontaneous pneumothorax, tension pneumothorax, sucking wound pneumothorax, pulmonary atelectasis, pulmonary edema, mediastinal emphysema and pulmonary embolism The prompt and correct diagnosis of these conditions and the proper treatment helps the physician to avert what might otherwise be a catastrophe.

PULMONARY HEMORRHAGE

Hemoptysis or pulmonary hemorrhage is an alarming symptom which is frequently present with pulmonary tuberculosis, bronchiectasis, benign or malignant tumors of the lung, mitral stenosis, pneumonia, pulmonary distomatosis (lung fluke disease due to Paragonimus westermanii), blood dyscrasias, polycythemia vera, pulmonary telangiectasis, pulmonary embolism or thrombosis, trauma to the thorax, pulmonary abscess, hypertension, cardiac failure, pulmonary emphysema and fibrosis, blast injuries and other conditions Hemoptysis is especially common in pulmonary tuberculosis and in about 50 per cent of the cases it occurs during the course of the disease In a previously well individual, the sudden onset of hemoptysis strongly suggests pulmonary tuberculosis Hematemesis is at times difficult to differentiate from hemoptysis but blood from the stomach is often acid, granular and dark, while blood from the lung is usually alkaline, frothy and produced with some coughing This part of the paper will deal only with the emergency treatment of pulmonary hemorrhage due to tuberculosis

The pulmonary hemorrhage of tuberculosis may be classified into three types as follows

1 Blood streaked or blood tinged sputum, probably produced by oozing from a hyperemic area of lung or ulcerated mucosa
2 Expectoration of a teaspoonful to several ounces of pure blood possibly recurrent This is the commonest form of bleeding and is caused by an ulceration or erosion of a blood vessel by the disease process
3 Massive hemorrhages, which are caused by destruction of the lung parenchyma which leaves the pulmonary vessels unsupported so that rupture occurs

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Death from drowning or suffocation is one of the dangers of pulmonary hemorrhage Spread of disease from one lobe of the lung to another is another complication Massive atelectasis and shock from hemorrhage are some of the other dangers of pulmonary bleeding

Treatment.—In the treatment of pulmonary hemorrhage the following measures should be applied· The patient should be reassured at once that bleeding is not unusual in pulmonary tuberculosis and that he should not be alarmed Initially, he is put at rest preferably flat in bed and advised not to talk or raise himself Coughing should be avoided as much as possible Codeine sulfate 0 016 gm (¼ grain) every four hours is usually sufficient to control the cough *Morphine and other powerful narcotics should be avoided since they reduce the cough reflex and depress respiration* The bronchial tree may thus become filled with blood and death from anoxemia results Phenobarbital 0 016 to 0 032 gm (¼ to ½ grain) every four hours helps to control restlessness and anxiety The patient should be put in an oxygen tent if any signs of cyanosis or anoxemia are present

When the patient is first seen, it is extremely important to try to determine the source of the bleeding He may have localized symptoms in one lung or the other, and rales may point to the source of the bleeding, but aspirated blood in the opposite lung may be misleading An x-ray examination of the chest usually reveals the diseased area of lung

The position in which the patient should finally be placed depends on the source of the bleeding and its severity Patients with only a slight hemoptysis can be treated safely in the semi-Fowler position with the bleeding side down With a slight to a moderate hemorrhage the patient should lie flat in bed, and turned on the bleeding side if it has been determined Patients with severe hemorrhage are best treated in the prone position with the foot of the bed elevated on blocks so as to facilitate the drainage of the blood from the lungs If the side of the hemorrhage in the lung is known the patient should be turned on that side

Postural drainage over the side of the bed should be resorted to promptly if the patient shows signs of anoxemia after a severe hemorrhage or after the ill advised use of narcotics in a moderate hemorrhage This procedure can be life saving at times as the following case demonstrates

CASE I —R. W , a 53 year old white man, was admitted to the Pennsylvania Hospital in August 1948 He had developed a pulmonary hemorrhage four days previously and at that time his family physician sought advice by phone We advised against moving the patient and suggested the use of phenobarbital 0 032 gm (½ grain) and codeine sulfate 0 016 gm (¼ grain) every four hours as necessary but warned against the dangers of morphine Notwithstanding this advice, four days later the patient was given sodium amytal 0 2 gm (3 grains) and subjected to a long ambulance ride A pulmonary hemorrhage began when he was only half way to the hospital A trained nurse who accompanied the patient administered morphine sulfate 0 032 gm (½ grain) On arrival at the hospital the patient was cyanotic and in shock He had a persistent hacking

cough and was bringing up large amounts of blood which seemed to catch in his throat and block his breathing

Examination revealed many wheezes in the left side of his chest and many rales in the right Because of his critical condition postural drainage over the side of the bed was instituted This cleared the blood and mucus from his bronchial tree. The patient was then placed prone in bed in an oxygen tent, with the foot of the bed elevated His condition improved immediately He was given penicillin as a prophylatic measure against infection and subsequently he did well, except for a minor pulmonary hemorrhage

In certain instances of persistent or recurrent moderate to severe hemorrhages, *collapse therapy* is indicated if the source of the hemorrhage can be localized Pneumothorax is the procedure of choice and it is usually effective unless pleural adhesions prevent the collapse of the bleeding area At times this can be corrected by pneumonolysis Pulmonary hemorrhage is the one indication for a rapid induction of pneumothorax, and 500 to 1000 cc of air is usually given at the initial treatment

Other forms of temporary collapse therapy include phrenic nerve crush which, if not entirely adequate, can be supplemented with pneumo peritoneum With chronic persistent hemorrhage, thoracoplasty or lobectomy may be indicated

The following case illustrates the value of pneumothorax in the control of a pulmonary hemorrhage when the source is known

CASE II —M L , a 29 year old white man, was admitted to the Pennsylvania Hospital on February 24, 1946 He stated that on December 30, 1945 he developed a cold and noticed a fleck of blood in his sputum on one occasion There after he was well until the night of February 10, 1946 when he had a sudden sharp cough and brought up two or three mouthfuls of bright red blood Two days later he had a similar episode During the ensuing days he brought up liquid blood in small amounts practically every day The patient was seen at home by one of us (D A. C) because of persistent bleeding A routine survey film taken several weeks prior to the episode of hemoptysis revealed a lesion in the right upper lobe typical of tuberculosis Localized rales were present in this area Four hundred cubic centimeters of air were introduced into the right pleural space at midnight of February 22 and repeated the next morning with control of the active bleeding The patient was then transferred to the Pennsylvania Hospital where his pneumothorax was maintained

A number of *drugs* have been advocated for the treatment of pulmonary hemorrhage and they may be classified in two groups drugs which promote coagulation of the blood and drugs which lower blood pressure The former include calcium, vitamin C and vitamin K and are of *no* value in dealing with pulmonary hemorrhage unless a specific deficiency is present Drugs which lower blood pressure are nitrites and their derivatives Nitroglycerin 0.3 mg ($\frac{1}{200}$ grain) under tongue or mannitol hexanitrate 0 032 gm ($\frac{1}{2}$ grain) by mouth may be given We do not believe however, that drugs have any beneficial effect, but they make excellent placebos

Food and fluid should be restricted for the first twenty-four hours until the danger of further hemorrhage has ceased The patient should be told to *avoid straining at stool* since it might cause a recurrence of the hemorrhage The stools should be kept soft by the use of *milk of magnesia* 15 cc ($\frac{1}{2}$ ounce) and mineral oil 15 cc ($\frac{1}{2}$ ounce) Transfusion is ordinarily not indicated but if the loss of blood has been excessive and signs of impending shock are present, *blood* or *plasma* should be given

After an attack of pulmonary hemorrhage, the patient should be given at least 1 to 2 weeks' rigid bed rest During this period and for a number of months thereafter, frequent x-ray examinations are indicated to see if there has been any spread of the disease process The patient can increase his activity slowly until he is back on the same therapeutic regimen as was observed prior to the bleeding

Summary.—1 Pulmonary tuberculosis is the commonest cause of pulmonary hemorrhage

2 Absolute bed rest is indicated Both physical and mental rest should be stressed, mild sedation with barbiturate is necessary

3 The position of the patient in bed depends on the severity and extent of the bleeding The patient should be placed with the bleeding side down If there is active bleeding, he should be placed in the prone position with the foot of the bed elevated

4 *Morphine and other powerful narcotics should be avoided* Coughing should be avoided and it can often be controlled with codeine sulfate 0 016 to 0 032 gm ($\frac{1}{4}$ to $\frac{1}{2}$ grain)

5 Pulmonary collapse therapy is indicated if the bleeding fails to stop under conservative measures, provided the source of the hemorrhage is known

SPONTANEOUS PNEUMOTHORAX

The term pneumothorax is used to designate the presence of air in the pleural cavity Spontaneous pneumothorax is caused by rupture of the visceral pleura which has been weakened locally by an underlying disease Air continues to escape from the rent until the lung collapses sufficiently to close the hole

When spontaneous pneumothorax occurs in a previously well individual, it is referred to as pneumothorax simplex or idiopathic spontaneous pneumothorax The majority of this group are healthy young individuals who are often athletes It is seen in the age group of 20 to 40 years, more often in males than females and is said to be more common in the right lung The usual mechanism is the rupture of an emphysematous bleb on the surface of the visceral pleura The development of emphysematous blebs is thought to be due to a congenital defect or more likely a healed scar from a previous infection causing a partial obstruction and a ball valve effect in a small pulmonary subdivision Rupture of the bleb results from sudden straining or coughing but sometimes it occurs spontaneously It has been reported in high altitude flying and is apparently due to hyperventilation and the change in atmospheric pressure Simultaneous bilateral pneumothorax has also been reported

but in most instances there is an interval between the two seizures The second pneumothorax results from the same cause as the initial one or from hyperventilation of the second lung

The symptoms of spontaneous pneumothorax depend largely on the speed and extent to which it develops In the typical case there is a sudden pain in the chest and difficulty in breathing and usually a dry hacking cough The pain may be referred to the shoulder, across the chest, or down over the abdomen and may simulate symptoms of an acute abdominal condition or coronory occlusion Signs of shock and circulatory collapse may appear, but this is unusual As the ruptured lung collapses the opening into the pleura usually closes, and the acute distress subsides

On physical examination there is usually limitation of motion on the affected side and the trachea may be deviated toward the normal side Tactile fremitus is diminished or absent The percussion note is hyperresonant, but this is often difficult to distinguish from the contralateral side where the percussion note may be hyperresonant due to relaxation of the underlying lung The breath sounds are diminished or absent on the affected side and exaggerated on the opposite side When there is a positive pressure pneumothorax the coin test is positive Occasionally in left-sided pneumothoraces there is a knocking sound heard over the precordium synchronous with the heart beat, varying with position and with the respiratory cycle This sound is known as a cardiac or pericardial knock It is quite different in character and not to be confused with the crunching sound of mediastinal emphysema Displacement of the cardiac dullness and apex beat away from the affected side, a sign that is more marked on expiration than on inspiration, is the so-called shifting apex or pendulum heart This finding is more easily demonstrable on fluoroscopy than on physical examination The chest roentgenogram is usually characteristic showing a fading out of the lung markings with a definite lung margin However, in routine inspiratory roentgenograms a small pneumothorax may be easily overlooked, whereas it would be obvious in an expiratory film

Treatment.—Spontaneous pneumothorax does not require any special treatment unless a tension or pressure pneumothorax has developed (see below) The patient's activity should be restricted until the ruptured visceral pleura heals and the lung re-expands, which usually occurs in three to six weeks Frequent fluoroscopic and roentgenographic examinations are necessary so that the course of the disease can be followed At times it is advisable to test the intrapleural pressure at regular intervals especially if the pneumothorax is slow in absorption or if positive pressures have existed In tension pneumothorax and frequently in simultaneous bilateral pneumothoraces immediate aspiration of air from the pleural cavity is indicated This is done with the standard pneumothorax apparatus with the water bottles reversed so that air can be sucked from the pleural cavity The quantity of air aspirated should be sufficient to relieve the symptoms and to reduce the intrapleural pressure

No drugs are of any proven value in the treatment of spontaneous

pneumothorax The avoidance of morphine and other opium derivatives should be stressed because of their depressing effect on the respiratory center Pneumothoraces recur in about 5 per cent of cases, and this usually requires special treatment There are two viewpoints as to the management of recurrent spontaneous pneumothorax The first is to maintain the pneumothorax keeping the lung collapsed, thereby favoring healing of the ruptured area The second method is to introduce material into the pleural sac that will cause a mild pleuritis which favors the formation of adhesions between the visceral and parietal pleura, and in this way prevents recurrences Various substances have been used such as sterile culture broth, 50 per cent glucose, 1 per cent silver nitrate, gomenol in oil, even powdered talc The least harmful and probably the best is blood plasma with small amounts of the patient's own blood added to it The possibility of infection is reduced by the addition of 50,000 units of penicillin to the plasma-blood mixture In rare instances surgical resection of that portion of the lung that contains the fistula tract is justifiable

Tension or Pressure Pneumothorax.—Any pneumothorax, regardless of its etiology, in which the intrapleural pressure is greater than the atmospheric pressure is called tension pneumothorax, positive pressure pneumothorax or valvular pneumothorax The margins of the ruptured lung form a valve that opens on inspiration and allows air to enter the pleural cavity and closes on expiration so that the air is trapped in the pleural space As the positive pressure in the pleural sac increases, the heart and mediastinum are pushed to the opposite side This positive pressure not only interferes with the respiration in the normal lung, but embarrasses the circulation by impeding the venous return to the heart

The signs and symptoms of tension pneumothorax are those mentioned under spontaneous pneumothorax only they are more marked The patient is in acute distress and is usually very dyspneic, sometimes cyanotic, and exhibits signs of shock and circulatory collapse The pain and clinical picture may simulate coronary occlusion or an acute abdominal catastrophe

Treatment.—*Decompression* of the positive pressure should be done at once and is performed in the following manner A one gallon sterile bottle is placed on the floor beside the patient's bed and filled four to six inches deep with sterile water or saline A sterile two hole rubber stopper is placed in the mouth of the bottle and a piece of sterile glass tubing long enough to extend 1 cm below the surface of the water is pushed through one of the holes in the stopper Sterile rubber tubing is then run from the upper end of the glass tube up to the patient and several extra feet of tubing allowed so that the patient can be moved about the bed A large area of skin in the region of the fifth and sixth rib in the midaxillary line on the involved side is thoroughly cleaned with a skin antiseptic Using 1 per cent procaine and a No 26 needle, a skin wheal is raised over the sixth rib and the procaine infiltration is continued over the top of this rib in the midaxillary line and down to the parietal pleura

A blunt No 16 needle with a stilet in place is inserted just within the pleural cavity The stilet is withdrawn and the upper end of the rubber tubing is attached by means of an adaptor to the needle hub Air will immediately begin to bubble from the end of the glass tube under the water In a short time the patient will feel and will appear to be quite comfortable The needle should be securely tied and taped in place so that the point will remain just inside the pleural cavity The needle can be removed when the air has ceased to bubble in the bottle, an indication that the valve in the visceral pleura has been sealed However, the decompression set should be kept at the patient's bedside in case of another emergency

Oxygen administered by tent, nasal catheter or mask is of value during the acute stage of tension pneumothorax and it should be immediately available if an emergency recurs during the hospital stay

CASE III —J K., a 25 year old white woman, was admitted August 1, 1940 to the Pennsylvania Hospital on the service of Dr P MacNeal Except for a chronic cough and a cold three weeks before admission the patient was well until five days prior to admission when she suddenly developed a sharp cramp-like pain in the lower anterior right chest while stooping over On the following day the pain had moved to the left of the sternum and recurred five to six times a day It usually lasted ten to thirty minutes and was aggravated by deep breathing

Examination of the chest on admission revealed a hyperresonant percussion note over the right side of the chest with distant breath sounds The patient continued to have pain in her left chest and increasing dyspnea. Distant breath sounds were noted at the left base on August 5 A chest x ray verified the clinical opinion that bilateral pneumothorax was present with a 40 to 50 per cent collapse on the right and a 30 to 40 per cent collapse on the left Physical examination on August 6 revealed the trachea slightly deviated to the left The cardiac dullness was obliterated Distant amphoric breath sounds were present over the lower half of the right lung field Breath sounds were practically absent over the left lung.

The patient's dyspnea gradually increased despite oxygen therapy and on August 10 the right pleural cavity was decompressed by means of a pneumothorax machine (5000 cc air removed) The needle was left in the right pleural cavity and connected with a positive pressure water trap at 1 cm of water pressure However, the patient continued to be quite dyspneic A needle was inserted in her left pleural cavity and connected with a water trap of 1 cm of water positive pressure Air bubbled through the trap and there was a prompt relief of her symptoms as the positive pressure in the left pleural cavity decreased Penicillin was started to prevent infection Later in the afternoon the needle was removed from the right chest since the positive pressure was no longer present

The needle in the left chest was not removed until August 11 The patient remained in the hospital until September 25 and both lungs were completely re-expanded

The patient remained in bed at home, but on October 12, 1946 she returned to the hospital for a chest x ray On the following day she began to have intermittent pain in her left chest which persisted She was readmitted on October 25 1946 and an x ray at that time verified the diagnosis of left pneumothorax

The lung was completely re-expanded on November 11, 1946 so the patient was sent home for bed rest

On December 14, 1946 there was some pain in the right chest followed by a right spontaneous pneumothorax On February 14, 1947 the left lung collapsed On March 12, 1947 she again had pain in the right chest She was admitted to the Pennsylvania Hospital where a bilateral pneumothorax was demonstrated On March 21, 1947, 150 cc of plasma, 5 cc of the patient's citrated blood and 150,000 units of penicillin in 8 cc of saline were introduced into the left pleural cavity The patient left the hospital on April 5, 1947

The patient was readmitted on May 18, 1947 because of a right spontaneous pneumothorax On May 20, 1947, 150 cc of plasma, 10 cc of the patient's citrated blood and 200,000 units of penicillin were introduced into the right pleural space She was discharged from the hospital on June 3, 1947

The patient was readmitted on July 19, 1947 with a right spontaneous pneumothorax She was again treated by intrapleural injection of plasma, citrated blood, and penicillin She appeared jaundiced the following day and a diagnosis of homologous serum hepatitis was made Investigation revealed that another patient who received the same plasma on March 21, 1947 also developed jaundice The patient was discharged on August 7, 1947

The patient was readmitted to the Pennsylvania Hospital on September 21, 1947 with a left spontaneous pneumothorax Plasma 150 cc and 10 cc of the patient's citrated blood were again introduced into the left pleural cavity, on October 29, 1947 a small right pneumothorax was present She was discharged on November 7, 1947 with the right lung completely expanded and the left lung almost completely expanded

Sucking Wound Pneumothorax.—Severe perforating injuries to the thorax will often result in a pneumothorax With each inspiration air will be sucked into the pleural cavity and expelled with expiration The opening in the skin should be covered tightly with a large sheet of sterile rubber-dam, sterile petrolatum gauze, or thick layers of sterile gauze After suture of the wound the air should be aspirated by continuous suction with a sterile catheter or blunt needle

Summary.—1 Emphysematous bleb formation is probably the commonest cause of spontaneous pneumothorax

2 The symptoms are sudden pain in the chest which may be referred to the abdomen, with dyspnea and a dry hacking cough

3 The signs are deviation of the trachea away from the pneumothorax, tactile fremitus diminished or absent in the affected side, a hyperresonant percussion note, and breath sounds diminished or absent on the affected side X-ray examination of the chest will confirm the clinical impression

4 Treatment of uncomplicated spontaneous pneumothorax is usually limited to bed rest

5 Bilateral spontaneous pneumothorax or tension pneumothorax is often an indication for immediate decompression of the pleural cavity

6 With repeated spontaneous pneumothorax, the involved lung can be maintained in a collapsed state by therapeutic pneumothorax treatments until the lesion heals Good results are also obtained by creating a pleuritis with a mixture of human plasma and citrated blood of the patient

7 Oxygen therapy should be used during the acute stage of spontaneous pneumothorax

PULMONARY ATELECTASIS

Pulmonary atelectasis is the collapse of lung tissue to a retracted, airless state. It can vary from collapse of a small lobule to collapse of a pulmonary segment, a lobe or at times an entire lung

There are a number of conditions which cause or are complicated by atelectasis, including lung infections, shock, pulmonary embolism and infarct, asthma, tumor of the lung or bronchus, and pressure on a bronchus by an enlarged lymph node or aneurysm Atelectasis was formerly a more or less frequent complication following major operations but with the recent advances in anesthesiology it is less commonly seen In preparation for surgical intervention patients are often heavily sedated and the cilia in their bronchial tree cease to function Heavy mucous accumulates in the bronchi because the cough reflex is depressed Because deep breathing often aggravates their pain, the respiration is shallow and any urge to cough is suppressed for similar reasons Abdominal distention frequently adds to the respiratory embarrassment by causing elevation of the diaphragm

The etiology of atelectasis can therefore be found in two conditions (1) an obstruction in the bronchial tree, or (2) some interference with the respiratory movement

The symptoms of atelectasis may be mild or severe The onset is usually rather rapid with dyspnea, orthopnea, cough, cyanosis and prostration The sputum is frequently mucopurulent in character Examination reveals that the patient has some varying degrees of fever and the pulse and respiration rates are rapid The affected side may appear smaller on inspection and the expansion is limited or absent In some cases there is actual retraction of the costal margin of the affected side on inspiration The trachea is usually deviated toward the involved side and the apex of the heart is always displaced toward the affected side Dullness is found on percussion over the atelectatic area The breath sounds vary but are usually recorded as distant, but not infrequently bronchial breathing is heard over the collapsed portion The diaphragm on the affected side is usually elevated Rales are usually present in adjacent areas

The roentgen ray examination shows a dense shadow over the airless portion of the lung The mediastinal structures are displaced toward the affected side and the diaphragm on the involved side is elevated

Treatment.—The treatment depends on the cause of the atelectasis and the degree of involvement For mild degrees of collapse and for prevention, conservative measures are often effective These include *deep breathing* and *coughing* exercises every half hour for five minute periods *Rebreathing in a paper bag* or the *inhalation of 5 per cent carbon dioxide and 95 per cent oxygen* are often effective measures The patient should be *turned every half hour* from one side to the other Oversedation

with morphine sulfate and other sedatives should be avoided *Early ambulation* when possible is indicated Initial therapy comprises the prophylactic administration of aqueous *procaine penicillin* 300,000 units every twelve hours intramuscularly

If these conservative measures fail or if the collapse is more marked, certain additional procedures are indicated *Aspiration of the trachea* is of benefit A firm, medium sized catheter (opening at the distal tip end) is lubricated with petrolatum and attached to a suction pump The suction should not be set higher than minus 5 to minus 10 cm of water A hole in the upper end of the catheter is valuable in permitting intermittent suction by covering the hole with a finger The catheter is then passed through one of the nostrils until it reaches the posterior pharynx as evidenced by gagging The patient is asked to breathe a little deeper and with the beginning of inspiration the tip of the catheter can usually be rapidly advanced through the larynx This causes a terrific paroxysm of coughing and an increase in cyanosis By turning the head to the left the catheter often can be passed down the right bronchus and similarly by turning the head to the right the catheter often will go down the left bronchus A great deal of mucus often can be aspirated, but the catheter should not be allowed to remain in the trachea too long since it often gives rise to a temporary laryngeal spasm and feels quite uncomfortable The main benefit from the procedure is the inducement of bouts of coughing which often will loosen the offending plugs of mucus After the procedure has been repeated several times, the patient should be allowed to rest.

In severe cases of atelectasis, a bronchoscopist should be called at once, since relief of the obstruction by aspiration of mucus through the bronchoscope is often life saving In children and in cases in which there is a suggestive history of foreign body or bronchial obstruction, *bronchoscopy* is indicated Chronic atelectasis should always be investigated by bronchoscopy because of the possibility of carcinoma of the lung

The prevention of atelectasis is most important after surgical operations Tight bandages around the chest and oversedation should be avoided Deep breathing, blow bottle exercises and frequent change of position in bed should be ordered The pharynx should be aspirated if secretions are collecting

Summary.—1 Pulmonary atelectasis is usually produced by bronchial obstruction or interference with respiratory movements

2 The symptoms are dyspnea, orthopnea, cyanosis, cough and fever

3 Physical signs are variable but there may be deviation of the trachea and apex beat toward the affected side, limitation of motion of the atelectatic side, dullness to percussion and bronchial breath sounds

4 The clinical diagnosis is confirmed by findings on x-ray examination

5 Prevention is the most important part of treatment and includes frequent change of position, avoidance of oversedation, and regular deep breathing and blow bottle exercises

6 Treatment calls for removal of the obstruction by coughing, suction

by catheter or bronchoscopy, the latter should be done at once if the patient is in poor condition or acute distress Oxygen and antibiotic therapies are indicated

PULMONARY EDEMA

The term pulmonary edema is used to describe the condition arising from the escape of serous fluid from the lung capillaries into the interstitial tissue, the alveoli and the bronchial tree This edema fluid interferes with the diffusion of oxygen to the lung capillaries so that anoxemia results This starts a vicious circle, the fluid causes anoxemia which in turn causes increased capillary permeability resulting in the extravasation of more fluid Pulmonary edema can be local or generalized, mild or fulminating The latter often leads to early death from suffocation

Left ventricular heart failure is a common cause of pulmonary edema There are probably a number of etiological factors at work, increased pulmonary blood volume and blood pressure, stasis, anoxemia, and increased permeability of the capillary walls resulting from vasomotor reflexes The latter may be the explanation for pulmonary edema which sometimes develops in shock, epilepsy or angioneurotic edema Pulmonary edema is also found in other allied conditions such as uremia, hypertension, nephritis, nephrosclerosis, drowning, pulmonary infarction or pulmonary embolism, and coronary thrombosis Acute pulmonary edema sometimes complicates infectious diseases, pneumonia and septicemia It has been suggested that a toxic effect on the vasomotor center controlling the lung vessels or collapse or failure of the circulatory system may be the cause Pulmonary edema also results from poisoning with alcohol, barbituric acid derivatives, iodine, morphine, epinephrine, asphyxiating gases, war gases, and following inhalation of industrial gases such as chlorine, bromine, phosgene and nitrous and nitric acid Pulmonary edema is also rarely reported in pregnancy, in diseases of the central nervous system, after abdominal and thoracic paracentesis, and after a general anesthetic

The attack of pulmonary edema may come on quite suddenly so that the patient and those about him may fear for his life The patient appears quite pale and perspires profusely His hands, feet and body feel cold He has a feeling of oppression in his chest Dyspnea, orthopnea and a short incessant cough are present Frothy fluid which is sometimes blood tinged may gush from the mouth Coarse bubbling rales are heard all over the lung fields The patient is terribly frightened and is often uncooperative and disoriented The prognosis in severe cases is quite grave

Treatment.—The treatment of pulmonary edema varies with the cause, and the precipitating factor should be determined and treated Patients with a tendency toward pulmonary edema should be treated with *bed rest* and *reassurance*, the body warmth should be maintained, a light *low sodium diet* (0.5 to 1.5 gm [7½ to 23 grains] of sodium chloride

daily) and *oxygen* should be given prophylactically In event of a severe anemia, a *blood transfusion* is indicated Morphine sulfate 0 016 gm ($\frac{1}{4}$ grain) should be given for the acute attack and repeated as necessary One hundred per cent *oxygen* by a B L B mask or by a positive pressure mask if available should be started at once A positive pressure between 2 and 5 cm of water is used at the beginning and the pressure is gradually lowered as the patient improves *Positive pressure should be avoided when shock exists*

Aminophylline 0 24 gm (4 grains) is of value when given intravenously in 10 to 20 cc of diluent The rate of injection should be quite slow and the administration through a small gauge needle should require at least five minutes Deaths have been reported following the use of many intravenous drugs including aminophylline, and a patient in pulmonary edema is an exceedingly poor risk

In hypertensive patients with heart failure and pulmonary edema, a rapid *venesection* of 250 to 500 cc is often of great value The use of three *tourniquets* which are rotated and used intermittently on the four extremities, fifteen minutes on and five minutes off, sometimes seems to be of value by temporarily holding large volumes of blood in the arms and legs Nitroglycerin 0 3 to 0 6 mg ($\frac{1}{200}$ to $\frac{1}{100}$ grain) also seems to be helpful in hypertensive patients

Weakness of the left ventricle, one of the commonest causes of pulmonary edema, should receive careful treatment If the patient has not received digitalis in the preceding four weeks, rapid digitalization is indicated Digitalis leaf 1 2 to 1 5 gm (18 to 23 grains) given in six divided doses at four hour intervals is quite effective Digitoxin 1 25 mg ($\frac{1}{50}$ grain) given in four divided doses at six hour intervals is sometimes employed Parenteral administration is required rarely and is recommended only for patients *in extremis*

Mercurial diuretics are of great value and should be given daily until the danger of pulmonary edema has passed Mercuzanthine 1 to 2 cc (15 to 30 minims) intramuscularly or intravenously is usually quite effective A *low salt diet* should be continued indefinitely *Aminophylline suppository* 0 45 gm (7 grains) at bedtime is quite effective in preventing noctural seizures of pulmonary edema

Summary.—1 Pulmonary edema commonly results from left ventricular heart failure but it is also seen in uremia, shock, infectious diseases and poisoning with sedatives, asphyxiating gases, and certain industrial gases

2 The onset of pulmonary edema may be rapid or slow and is characterized by dyspnea, orthopnea and a short incessant cough The patient appears pale and is perspiring profusely The lung fields are filled with coarse bubbling rales and frothy fluid may gush from the mouth

3 The cause of the attack should be determined and treated in the proper manner Therapy includes 100 per cent oxygen by positive pressure mask, morphine sulfate 0 016 gm ($\frac{1}{4}$ grain) hypodermically, and aminophylline 0 45 gm (7 grains) slowly intravenously Reassurance is quite important

MEDIASTINAL EMPHYSEMA

The term mediastinal emphysema is used to describe the presence of air in the mediastinum The etiology is from emphysema surrounding an atelectatic area Spontaneous mediastinal emphysema is due to a ruptured alveolus, with the air dissecting along the pulmonary vessels

Mediastinal emphysema may develop as a result of penetrating or nonpenetrating injuries to the chest, surgical operations on the thorax or neck, positive pressure anesthesia, pneumothorax, pneumoperitoneum, and severe coughing spells

The pain may simulate that of coronary occlusion but is made worse by deep breathing

Hamman's sign, a loud crunching or crackling sound synchronous with the heart beat, is found in most cases of mediastinal emphysema

Treatment.—Treatment other than *rest in bed* and *penicillin therapy* (300,000 units of aqueous procaine penicillin daily) is not indicated unless accompanied by a tension pneumothorax

CASE IV —N M , a 52 year old white man, was admitted to the Pennsylvania Hospital on September 1, 1941 because of central nervous system syphilis He was treated with fever therapy and, after his fifth treatment, sudden scrotal edema developed The patient developed a slight fever and subcutaneous emphysema over the left side of his body A positive Hamman's syndrome was demonstrated An x ray film of the chest revealed mediastinal emphysema and a small localized area of atelectasis at the right base Retroperitoneal air which outlined the iliopsoas muscles and kidneys was demonstrated The patient made an uneventful recovery

Summary —1 Mediastinal emphysema may result spontaneously as a result of rupture of pulmonary alveoli adjacent to an area of atelectasis

2 The important symptom of mediastinal emphysema is a sharp substernal pain which is made worse by breathing

3 Hamman's sign is a loud crunching noise that is synchronous with the heart beat

4 The treatment is bed rest and penicillin therapy

PULMONARY EMBOLISM

The term pulmonary embolism is used to describe the migration and lodging of a blood clot in one of the pulmonary arteries or arterioles A pulmonary infarct does not result unless the collateral circulation is impaired The blood clot usually originates in the veins of the feet, the deep veins of the legs, the pelvic veins, or the right auricle in cases of auricular fibrillation Dislodgement of emboli from these sources occurs during straining when there is a rapid change in venous pressure

The symptoms of pulmonary embolism vary considerably but usually consist of sudden, severe pain in the chest, dyspnea, orthopnea, hacking cough, bloody sputum and, frequently, signs of collapse The patient appears anxious, pale, cyanotic, and sweats profusely There may be few physical findings other than tachycardia unless a peripheral part of

the lung is involved Frequently, however, a friction rub is audible and a local area of dullness, crackling rales and bronchial breath sounds are elicited Fever and leukocytosis usually develop

Treatment.—The treatment of pulmonary embolism consists of *oxygen therapy* by nasal catheter, oxygen tent, B L B mask, or a positive pressure oxygen mask Morphine sulfate 0 016 gm (¼ grain) should be given at once The intravenous injection of *papaverine hydrochloride* 0 03 gm (½ grain) may help to relieve the spasm of the pulmonary vessels and bronchi *Stellate ganglion block* on the involved side is considered to be of value *Procaine hydrochloride*, 1 gm dissolved in 1000 cc. of 5 per cent dextrose solution, has been effective when given intravenously in relieving vascular spasm due to an embolus involving the arteries of the extremities The administration of procaine hydrochloride is not recommended in cases of pulmonary embolism since serious side reactions often develop However, in one massive case of pulmonary embolism at the Pennsylvania Hospital, procaine hydrochloride intravenously resulted in a dramatic relief of symptoms

The most important part of the therapy of pulmonary embolism is the prevention of subsequent embolism from the original source The details of anticoagulant therapy are described in Dr David Marshall's paper (see page 1501)

Summary.—1 Pulmonary embolism is caused by a blood clot lodging in the pulmonary artery The source of the blood clot is usually a foot vein, a leg vein, a pelvic vein, or the right auricle of the heart

2 The symptoms of pulmonary embolism are sudden pain in the chest, dyspnea, orthopnea, hacking cough, bloody sputum and profuse sweats

3 The signs are variable but typically consist of a local friction rub, dullness to percussion and crackling rales, and bronchial breathing, fever and leukocytosis are common

4 Treatment consists of oxygen therapy, morphine sulfate 0 016 gm (¼ grain), and the intravenous injection of papaverine hydrochloride 0 032 gm (½ grain) Anticoagulant therapy is indicated

THE TREATMENT OF SOME ACUTE RHEUMATIC DISORDERS

RICHARD T SMITH, M D *

In the majority of rheumatic disorders, spasm of muscles is responsible for a considerable degree of the disability, discomfort and loss of function It may be produced by exposure to excessive heat or cold, overextension of the muscle, sprains or strains, direct injury, overindulgence in unaccustomed activity, and atrophy of muscle Spasm caused by any of these factors may have an acute, subacute or a gradual onset, manifested by any degree of disability from mild stiffness to severe limitation of motion of the joint Spasm of the muscle is often of short duration, disappearing spontaneously if it can be dissociated from pain However, the realization that immobilization relieves pain may initiate what might be termed "habit spasm," within a matter of hours or days The transition from ordinary spasm to "habit spasm" ordinarily occurs without the knowledge of the patient The original disability may then be continued indefinitely, and the condition may change from an acute one to a chronic disability characterized by "habit spasm," voluntary limitation of motion, shortened tendons, actual limitation of motion, and disability, all associated with pain This is illustrated by the patient with acute subdeltoid bursitis who, though improved, has residual limitation of motion with pain months later

Physiatrists are aware of the part spasm of muscle plays in many acute musculoskeletal disorders, so that often more attention may be given to the secondary spasm of muscle than to the original cause of the acute disability Treatment directed toward correcting spasm of muscle associated with acute bursitis, lumbago, sacroiliac strain and sprain, lumbosacral joint difficulties and sciatica frequently relieves painful symptoms and gives a normal range of motion in a shorter time as compared with treatment directed at correcting the so-called underlying condition

THE ALLEVIATION OF MUSCLE SPASM

Many methods of treatment are used to alleviate muscle spasm, including the administration or prostigmine, physostigmine, eserine procaine, curare, heat, massage, passive and active exercises, and various types of electrical current All afford varying degrees of improvement depending upon the type of difficulty and the patient's condition, but none of these methods give completely satisfactory results However, new drugs such as 'Tolserol' promise more far reaching benefit either alone or in conjunction with other therapeutic measures

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Tolserol.*—Tolserol relaxes spasm of muscle without paralysis The margin between therapeutic and lethal doses is wide, making it safe Tolserol was first used in solutions ranging from 2 per cent to 10 per cent for intravenous administration Higher concentrations caused hemolysis but 2 per cent solutions were found to be relatively safe This drug is available in tablets and capsules containing 0 25 gm The average dose is 0 023 gm per kilogram of body weight, e g , persons weighing 59 to 70 kg are usually given six tablets as the initial dose, 71 to 84 kg , seven tablets, 85 to 90 kg , eight tablets and over 91 kg , nine tablets An initial test dose given under the direct observation of the physician is advisable The range of motion, spasm of muscle and pain are evaluated before and thirty to forty-five minutes after the test dose The maximum relaxation of muscle usually develops within forty-five minutes and may be maintained by giving one tablet every two hours or two tablets every three hours throughout the day This plan of therapy is followed each day while necessary, the initial dose being repeated each morning with smaller amounts at two or three hour intervals In many instances an acute spasm of muscle may be relieved with one dose

Failures occurred with this drug in selected cases where improvement might be anticipated In a high proportion of these instances it is believed that the failure was due to faulty absorption of the drug In preliminary tests, with intravenously injected Tolserol, relaxation occurs in such selected cases tending to substantiate this concept

Certain side effects occur which are believed to be necessary in order to have an adequate result These are a feeling of warmth of the face, or the entire body and a sense of impending dizziness The latter has been variously described as dizziness, lightheadedness, or "floating on a cloud " These effects are of short duration, and the latter has not been observed to continue to a degree causing a state of dizziness, instability, staggering or reeling

Tests of strength of muscle indicate that there is no loss of control of muscle or strength following the use of Tolserol, suggesting the administration of the drug just prior to physical therapy or exercise periods By relieving stiffness and discomfort, a better range of motion is possible and more nearly normal function is permitted, thus hastening clinical improvement

It is believed that Tolserol acts on the brain stem inasmuch as there is relaxation of muscle and partial relief of pain In experiments with animals larger doses than those recommended in this paper have shown an effect upon the spinal cord and very large doses have produced paralysis in animals

Compound E and ACTH.—Compound E (17-hydroxy-11-dehydrocorticosterone), an adrenal cortical hormone, and ACTH, the pituitary adrenocorticotropic hormone, have been reported capable of producing rapid remission of symptoms in rheumatoid arthritis, rheumatic fever

* "Tolserol" is a trademark of E R Squibb & Sons, known in Europe as "Myanesin "

and lupus erythematosus ACTH has also controlled attacks of gouty arthritis Rheumatoid spondylitis has responded to treatment with synthetic estrogens The discovery of the "reversability of symptoms" in rheumatoid arthritis, rheumatoid spondylitis, rheumatic fever, gouty arthritis and lupus erythermatosus following therapy with hormones opens a new field of investigation *Compound E and ACTH may produce* serious undesirable reactions They are difficult to synthesize, scarce and expensive, limiting their use in rheumatic diseases at present

Salicylates.—In treating rheumatic disorders, it is recommended that salicylates in adequate doses be used alone, rather than with narcotics, because many of these conditions become chronic requiring prolonged therapy A minimum of 0 6 gm (10 grains) of acetylsalicylic acid or sodium salicylate *every three or four hours* is used to relieve discomfort Occasionally codeine 0 01 to 0 016 gm ($\frac{1}{6}$ to $\frac{1}{4}$ grain) may be used with salicylates Salicylates should be used even when the pain is mild, in order to afford relief and permit better function

Physical Therapeutic Measure —Physical therapeutic measures are an important part of the program of treatment for rheumatic diseases *Heat*, usually followed by massage may be applied every day in the home in inexpensive ways, e g , heat lamp, heating pad, hot paraffin, electric iron, hot bricks, hot sand, gas and electric heaters or ovens At least one daily period of therapeutic *exercise* should be preceded by heat and massage since better function of muscle is made possible Household measures are most beneficial when supplemented by professional physical therapy two or three times a week Passive exercise (involuntary *joint motion performed by another person) is used when muscles are* too weak to perform the functions of the joints Active assistive exercises (a combination of voluntary and involuntary motion of the joint) are instituted to aid muscles capable of a limited range of motion by passively increasing the extent of flexion and extension Active exercise is voluntary motion of the joint without assistance

It is essential to take the time to instruct each patient in the mechanics of the disability and the need for each part of the program of treatment Education of the patient in his disease will assure better cooperation and benefit from the therapy employed

SUBDELTOID AND SUBACROMIAL BURSITIS

The acute or chronic inflammation in these conditions initiates varying degrees of spasm of muscle as a protective mechanism Spasm increases the discomfort brought on by the inflammation and attempts to move the involved part are met by increased spasm of muscle and pain The following program is of value in therapy An explanation of the cause of the condition is given to the patient emphasizing that the *secondary spasm of muscle is increasing the discomfort* and prolonging the disability

Treatment in an Acute Attack.—Tolserol (0 023 gm per kg of body weight) is followed by twenty to thirty minutes of therapy with heat

usually in the form of diathermy, after this ten to fifteen minutes of massage of the muscles in proximity of but not overlying the affected bursa The patient is then given passive (involuntary) exercises on the shoulder wheel for five to ten minutes At the end of this time, active assistive (voluntary plus involuntary) followed by active (voluntary) shoulder wheel exercises are encouraged The action of the Tolserol can be prolonged by giving 0 25 to 0 5 gm at two or three hour intervals Salicylates 0 6 to 1 3 gm (10 to 20 grains) every four hours are given concurrently The treatment is most effective when carried out daily and usually gives excellent results within a period of one to five days

Therapy with roentgen rays often results in prompt relief of pain when applied to an acutely inflammed bursa Local infiltration of the painful area and/or block of the suprascapular nerve with a local anesthetic frequently relieves pain for hours to days Therapy with roentgen rays and local anesthetics are not recommended to the exclusion of other measures but as a part of a program of treatment

Case Report—E R S , aged 62, a grave digger, dug two graves on April 4, 1949 At about 4 A M on the morning of April 5, he was awakened with severe pain in the right shoulder, so that any motion beyond 15 degrees of abduction was very painful Examination the same afternoon revealed exquisite tenderness over the right subdeltoid bursa and severe spasm of the muscles of the upper arm and about the shoulder Forty-five minutes after taking 1 75 gm of Tolserol there was relaxation of spasm and motion was possible to 30 degrees of abduction Diathermy was applied to the right shoulder for twenty minutes followed by massage of the muscles about the shoulder but not over the bursa for ten minutes Shoulder wheel exercises were then given for twenty minutes beginning with the passive type During the last three minutes complete revolutions of the wheel were possible with only slight discomfort Therapy with Tolserol was continued as outlined above and the same program was carried out daily for four days On the fifth day he dug a grave with no discomfort in the shoulder

Treatment of a Chronic Attack —Weeks or months after the onset of bursitis the patient may still have severe limitation of motion of the arm involved, with discomfort in moving the arm beyond a very restricted range In these instances the causes of restriction of motion are usually chronic "habit spasm" and shortening of the tendons The acute inflammation in the bursa is no longer present and it is the secondarily limited motion which must be corrected

Therapy with Tolserol will permit a slight increase but not complete range of motion Nevertheless, Tolserol is recommended supplemented by therapy with heat, applied to the shoulder in the form of diathermy and massage Passive, active assistive and active shoulder wheel exercises are then given as described above

As an adjunct in the therapy for this chronic disability, *interrupted sinusoidal current* is helpful This is applied in the following manner A large inactive electrode is placed across the midline of the back at the juncture of the thoracic and lumbar regions The small active electrode is applied to the lower portion of the biceps muscles for ten minutes and

then the lower portion of the triceps muscles for ten minutes If there is evidence of limitation of motion of the supraspinatus tendon, this muscle should also be treated with interrupted sinusoidal current The frequency of contractions are limited to sixteen to twenty-eight contractions per minute, and the intensity of the contractions should be kept within the limit of comfort, but gradually increased according to the tolerance of the patient Interrupted sinusoidal current may be given directly after the diathermy or may be alternated with the diathermy Physical therapy should be carried out every day if possible In addition, the patient is taught shoulder exercises to be done at home every day after therapy with heat, using an infra-red lamp for thirty to forty minutes before each exercise period as well as prior to the physical therapy treatment Gradual improvement will be noted over a period of several weeks It is necessary to carry out the treatment for four to six weeks depending upon the duration of the limited motion following the bursitis

DISCOGENETIC DISEASES OF THE CERVICAL SPINE

Discogenetic disease signifies a condition of the cervical spine where a combination of osteoarthritic changes encroaching upon the posterior foramen and narrowing of the intervertebral disk spaces cause intermittent or chronic pressure on the roots of nerves It may be characterized by recurrent acute attacks of pain of a few hours' or a few days' duration or the disability may become chronic in nature There is usually evidence of pain radiating into one arm or the other and less frequently to both, over all or part of the branches of the brachial plexus This includes not only pain in the arm but pain over the posterior portion of the shoulder and over the lateral wall of the chest The distribution of the pain is dependent upon the location of the nerve root pressure Roentgenograms of the cervical spine frequently show narrowing of the intervertebral spaces often with osteoarthritic changes on the posterior margin of the vertebral body and encroaching upon the posterior foramen There may be sclerotic changes in the facets of the cervical spine Examination usually reveals tenderness over the nerve roots the brachial plexus and the involved nerve trunks in the arm or the wall of the chest or over the suprascapular nerve depending upon which roots are involved This condition is ordinarily associated with poor posture manifested by forward protusion of the neck, increased dorsal kyphosis, and relaxation of the abdominal wall History of recurrent stiff neck is not uncommon

Recurrent acute attacks can generally be relieved within an hour with the usual dosage of Tolserol (0 023 gm per kg of body weight) It is advisable however, to continue the medication for two to four days *This treatment alone has no effect upon the underlying condition which is responsible for the recurrent attacks*

Mechanically there is narrowing of the intervertebral space which decreases the size of the posterior foramen and thus tends to produce

pressure of a recurrent or chronic nature upon certain nerve roots Mechanically, this process may be reversed by the following treatment

1. Tolserol, 0 023 gm per kg every morning followed by 0 5 gm every three hours for a period of two weeks

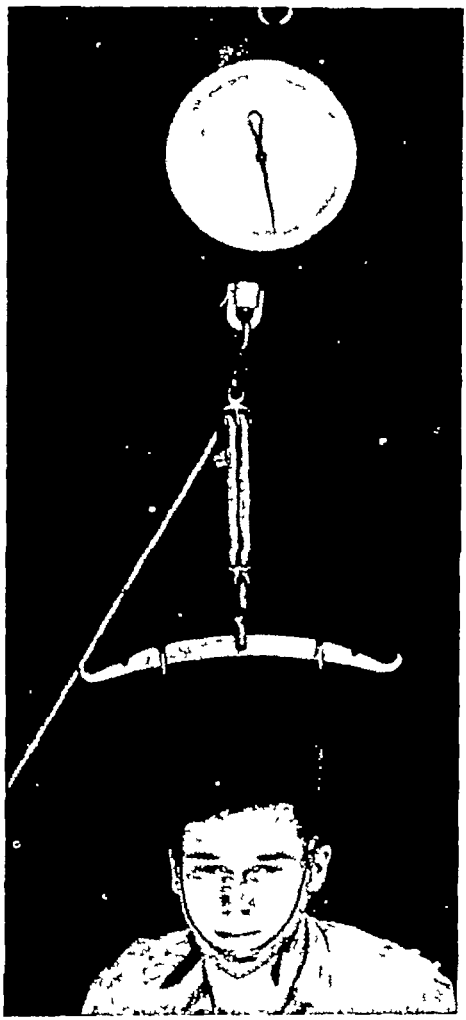

Fig 264 —Sayre halter —From top to bottom the apparatus consists of a scale, an S hook connecting to the upper pulley of a double pulley system, the pulley system, an S hook connecting the spreader bar to the lower pulley, the halter apparatus attached to the spreader bar The halter fits under the chin and firmly under the occipital region and is maintained in these positions by side straps which are adjustable This apparatus may be hung from a doorway or from a rafter in a basement or garage The number of pounds of traction are read directly off the scale A patient may treat himself by placing a mirror before him to read the scale

2 Twenty to thirty minutes of baking of the posterior portion of the neck with infra-red heat, two times daily
3 Following the heat, neck traction is carried out with the Sayre halter (Fig 264)

The initial traction with the Sayre halter should not be more than 35 to 40 pounds Traction is applied for a period of thirty to sixty seconds and then eased This is to be carried out two or three times at each sitting The traction should be increased gradually approximately 5 pounds during the first week, within the next three days another 5 pounds, and 5 pounds additional every three days until not more than 70 pounds traction is used In the presence of severe chronic spasm of muscle the increments of increase may require modification particularly if any increase in traction causes pain in the neck Thus, by the end of three weeks 70 pounds traction should be the standard for each treatment in most instances It is possible to increase the length of time the traction is applied to over 60 seconds after two weeks of therapy The treatment will be more successful if carried out twice a day in the home After four weeks of this program the traction should be applied two or three times a week using 60 to 70 pounds of traction Sayre halter traction is contraindicated when vertebrae are fused by ligamentous or post-traumatic calcification since these may be fractured by the treatment

4 Throughout this program of treatment, postural exercises practiced daily improves the posture and relieves the strain that has been placed upon the muscles of the neck

Usually the patient notices relief from pain within several days after the treatment has begun, but this prolonged period of treatment is necessary in order to permit whatever re-expansion is possible of the compressed disks, and to overcome the "habit spasm" In the case of recurrent acute attacks, the same method of treatment is necessary to correct the underlying difficulty

LOW BACK PAIN

Low back pain may be acute or chronic Causes of low back pain are probably legion, but in almost every instance there is direct or indirect muscle involvement which increases or prolongs the disability and discomfort

The most common rheumatic causes are

1 Static and postural abnormalities
2 Lumbago (fibrositis of the lower back)
3 Trauma producing muscular, lumbosacral or sacroiliac strain
4 Rheumatoid spondylitis

Neuritis (sciatic, anterior crural, etc) is frequently found accompanying low back pain The exact mechanism is often obscure, but in many instances it is relieved by relaxation of muscle spasm of the paravertebral muscles

Static and Postural Abnormalities.—Very few persons have a good posture Even those with an average posture usually exhibit relaxed abdominal muscles, increased lumbar lordosis and forward tilting of the pelvis This position is conducive to increased dorsal kyphosis, flattening of the anterior wall of the chest, drooping of the shoulders and forward tilt of the head

Good body mechanics are exhibited when an individual is lying flat on the back on a firm surface, such as the floor, with the abdomen retracted, the pelvis tilted backwards (rolled under) and breathing with little or no abdominal motion Leg exercises in this position will strengthen the abdominal and lower paravertebral muscles Such postural exercises should be practiced for five to ten minutes, three or four times a day until a good posture is achieved, then once daily thereafter The patient is taught to become "abdomen conscious," by developing a habit of retracting the abdominal wall while standing, walking, sitting and lying Any shortening of a leg greater than $\frac{1}{4}$ inch should be overcome by shoe correction

Bad working habits frequently cause postural pain and strain These should be investigated and corrected whenever possible

Lumbago (Fibrositis of the Lower Back).—Lumbago usually has an acute onset In some instances, unilateral sciatica will be present Treatment consists of relaxation of muscle spasm, exercise and relief of pain

Salicylates in minimal doses of 0 6 gm every three to four hours should be given both for comfort and to permit better cooperation of the patient in the program of treatment Relaxation of muscles may be obtained by giving Tolserol (0 023 gm per kg of body weight) with a maintenance dosage (0 5 gm every three hours) until symptoms clear Therapy with heat (infra-red lamp) should also be used for twenty to thirty minute periods several times a day followed by deep massage Diathermy may be used except when sciatica is present Symptoms of sciatica may be intensified if diathermy is used Interrupted sinusoidal current with a frequency of contraction from 16 to 28 per minute will be helpful in combating muscle spasm, especially if there is an associated sciatica Body mechanics exercises should be done following muscle relaxation even though some spasm still exists

Case Report —H K., aged 60, a stationary engineer (light work), shoveled considerable snow on December 27 The next morning upon arising there was severe stiffness and moderate aching of the lumbar region, mild tilting of the trunk to the left and moderately severe pain radiating down the left leg to the foot in a sciatic distribution Symptoms persisted for two days, in spite of complete bed rest Examination on December 29 revealed severe spasm of the paravertebral muscles in the left lumbar region, tilt of the trunk to the left, and tenderness over the left sciatic nerve Thirty minutes after 0 023 gm of Tolserol per kg of body weight was given, muscle spasm subsided and a relaxed, erect posture was possible Mild aching persisted in the lumbar region and along the sciatic nerve Twenty minutes of infra-red heat therapy and ten minutes of massage were applied to the lumbar region Aching in the sciatic nerve persisted Interrupted sinusoidal current was then applied for twenty minutes with the large inactive electrode placed across the midline in the upper lumbar region and the small active electrode applied to the sole of the left foot Tenderness and aching of the sciatic nerve was completely relieved On December 30, mild aching was present in the lumbar region and in the left leg The same therapy was again applied No further discomfort was experienced On May 10 and 11 the patient worked in his garden Symptoms recurred on May 12 The same program was instituted and he was completely relieved in two days

Trauma Producing Muscular, Lumbosacral or Sacroiliac Strain — Strain of this nature generally follows some unusual motion and is frequently accompanied by a clicking or tearing sensation or sound or a feeling that "something slipped" The primary requisites of treatment are rest on a firm surface and support of the affected structure

Rest in bed for several days is very helpful Lying on the back with a small pillow under the knees, or on the side, or face down with the pillows under the hips will ease the strain on the affected part Continuous heat with a heating pad or hot fomentations will be beneficial Analgesics to relieve the discomfort are indicated A back support extending several vertebra above and below the painful area permits early ambulation Adhesive strapping, corset or brace may be used However, support should not be continued over too long a time or muscle atrophy will develop If spasm of muscle persists after the acute phase has subsided, Tolserol (0 023 gm per kg of body weight) with maintenance dosage (0 5 gm every three hours) should be instituted Body mechanics exercises must be practiced

Rheumatoid Spondylitis —Rheumatoid spondylitis frequently is characterized by repeated attacks of low back pain X ray therapy is the treatment of choice The therapy is directed over the area roentgenographically and/or clinically involved Body mechanics exercises are employed to correct postural defects, and measures for the relief of pain and muscle spasm are included

The spine should be divided into four areas for x-ray treatment, namely (1) the sacroiliac joints and lumbar spine, (2) the lower half of the dorsal spine, (3) the upper half of the dorsal spine and (4) the cervical spine Roentgen therapy should be applied every other day to one or more areas in divided doses Each area is to receive a total of 150 to 600 roentgen units Such a course of x-ray therapy may be repeated at any time after thirty days if symptoms recur Salicylates are required in sufficient doses to decrease the pain and stiffness Tolserol (0 023 gm per kg of body weight) with maintenance doses (0 5 gm every three hours) has been very successful in the management of this disease Relief from muscle spasm and pain has been noteworthy Heat, massage and interrupted sinusoidal current relieves discomfort and assists in the relief of muscle spasm during the acute phase of disease Body mechanics exercises should be instituted as soon as possible within the limits of pain

SYMPOSIUM ON NUTRITIONAL DISORDERS
From the Philadelphia General Hospital

FOREWORD

All life depends on food This simple fact is often overlooked in the rapid progress of *scientific* (i e., laboratory) medicine Too often the practicing physician leaves his patients only with the admonition to "Eat a light diet"—indeed if any dietary advice is given at all

The late war has by necessity forced scientists to study further the entire wide field of nutrition It now extends as a boundless field into every corner of medicine

Nutrition is intimately connected with endocrinology and with metabolism, it appears in the daily management of the medical and surgical patient, it is vital in our understanding of growth in children and the degeneration of old age Signs of nutritional abnormalities are detected by every means at our disposal, from the electrocardiogram and the roentgenogram, to the ophthalmoscope and the chemical laboratory

Yet nutrition as a science (as differentiated from dietetics) has been sadly neglected in most medical schools and textbooks of medicine, and it has been practically ignored in intern training

The papers forming this symposium all come from the Philadelphia General Hospital Here an unexcelled opportunity exists to study malnutrition in all ages, in all stages and of every conceivable variety We have attempted to summarize important and recent developments in clinical nutrition

It is to the practicing clinician, whose patients always ask, "What may I eat?" that the following papers are dedicated It is our hope that they may be of some benefit and assistance in managing the sick person For in every illness nutrition is disturbed, and disturbed nutrition will lead to illness

S O Waife, M D

DIETARY MANAGEMENT IN HEART DISEASE WITH PARTICULAR REFERENCE TO CONGESTIVE CARDIAC FAILURE

WILLIAM G LEAMAN, JR, M D, F.A C P *

During recent years a greatly increased amount of information has been made available in the science of nutrition Today a knowledge of these facts and their application is a prerequisite for the treatment of disease For example, the routine practice of giving convalescent patients first liquids, then soft, semisoft and finally solid diets has long since passed into the discard In modern practice, the dietary prescription is based on the clinical evaluation of the patient as well as the results of carefully selected laboratory procedures

The principles underlying the dietary management in heart disease, particularly in the presence of congestive cardiac failure, have been completely revised during the past two decades It is our purpose in this presentation to review them and to suggest, so far as possible, preventive and therapeutic dietary measures based on fact

GENERAL CONSIDERATIONS

A few general rules can still be applied to all types of heart disease Excessive body weight requires the heart to perform unnecessary additional work Therefore, the obese patient should be given a low-caloric diet whenever possible Optimum body weight is the goal The speed of its attainment will depend upon the age, type of heart disease present and the clinical status of each patient In prescribing a weight-reduction program, care should always be taken to avoid deficiency of important dietary constituents, especially vitamin B

Excessive food intake at one meal also increases the work of the heart and should be avoided by all cardiac patients Highly seasoned and bulky foods are not advisable, on the basis of what has been learned during recent years regarding active reflex pathways between the digestive tract and the coronary arteries [1]

CORONARY ARTERY DISEASE

The role of cholesterol in the pathogenesis of coronary artery disease is still controversial In this condition the main lesion is in the intima and should be referred to as atheromatosis rather than arteriosclerosis Cholesterol deposits in the intima are common in those patients whose

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blood cholesterol levels are elevated, although, so far at least, the lipid content of the diet has not been shown to stand in direct relationship A fertile field for future study would be the effect of a high-fat (peptic ulcer) diet on middle-aged men suffering from peptic ulcer alone This group should be contrasted to a large series of cases in whom peptic ulcer and coronary disease coexist Plotz[2] has already presented some thought-provoking evidence concerning the effect of high cholesterol diets in the latter group Ten patients are mentioned in whom death followed within several months after starting a diet high in fats In another small group (seventeen patients) the symptoms of coronary disease became worse in three months after a high-fat diet was instituted

Enough evidence has accumulated to date to cause thoughtful physicians to avoid prescribing a high-fat diet, even if low in cholesterol, for peptic ulcer patients who have coronary disease, particularly if the family history reveals other examples of either hypertensive or arteriosclerotic heart disease The same holds true for patients with diabetes, myxedema, xanthomatosis and hypercholesterolemia The observations of physicians in the Low Countries during the occupation in World War II showed a steadily decreasing incidence of myocardial infarction when diets exceedingly low in fats were given for long periods of time Among other races where the diet is low in cholesterol, particularly the Chinese, coronary atherosclerosis is rare

In clinical practice at the present time a determination of the blood serum cholesterol level seems worthwhile in all patients suffering from progressing coronary atherosclerosis If this value is found to be high, it may be wise to exclude from the diet foods that are rich in cholesterol, such as eggs, butter, cream, duck, brain, liver, sweetbreads, fat meats and sausage We should keep in mind that a low-cholesterol diet, if continued over a long period of time, may result in vitamin A deficiency since foods that provide the largest amount of vitamin A are high in cholesterol In prescribing this dietary restriction, we should never do so with an air of finality but should remain critical of the supporting evidence since the premise is so alluring

CONGESTIVE CARDIAC FAILURE GENERAL CONSIDERATIONS

Its Nature and the Mechanism of Its Production.—At the present time there is not complete agreement among physicians as to what constitutes cardiac failure and the mechanism by which it may occur in the patient with heart disease Starling and Visscher[3] have probably best defined the situation as "that state in which the normal mechanical work of the heart cannot be maintained unless oxygen consumption of the heart muscle increases and venous pressure rises " One group of clinicians is of the opinion that heart failure and its symptoms are the result of back pressure in the central veins, with subsequent increase of venous pressure in the pulmonary and peripheral circuits [4] This is the so-called "backward failure" which accounts for the clinically apparent venous engorgement, hepatomegaly, pulmonary rales and peripheral edema

Opposed to this theory is that proposed by another group who believe that "forward failure," characterized by an inadequate cardiac output with consequent reduction in oxygen supply to tissue (particularly renal) will account for the changes noted in cardiac failure Merrill[5] points out that when cardiac output has been reduced to one-half normal, renal blood flow is reduced to one-fifth normal Though evidence is accumulating to support the theory of "forward failure," it is reasonable to believe that both concepts, forward and backward, contribute to the pathologic state which we term "cardiac decompensation" Certainly there are those cases of failure in which the minute volume of the heart is but little reduced, while further consideration of backward failure reveals that forward flow persists despite decompensation In any event we must conclude that in congestive failure cardiac output is not sufficient to maintain bodily requirements, whether at rest, during exercise, or during any state which imposes additional stress upon the heart

Many investigators have postulated that the edema of heart failure is a result of increased capillary permeability due to a diminished oxygen supply to the tissues Warren and Stead,[6] examining edema fluid from patients with congestive failure, found very little protein in the specimens and concluded that neither lymphatic obstruction nor increased capillary permeability were significant factors in the production of cardiac edema Their further investigations[7] suggested that the probable mechanism of edema formation was more likely on the basis of disturbed renal function produced by heart failure in which fluid intake exceeds the fluid output

Peters,[8] in discussing the renal excretion of water, suggests that when water is administered to a healthy individual the concentration of serum water is increased, while the salt content is diminished to such an extent that the kidneys are stimulated to excrete more than the usual amount of urine. On the other hand, the use of normal saline instead of water does not stimulate renal excretory activity because the composition of the serum is not appreciably altered

In the case of congestive heart failure, the ability of the kidney to excrete sodium and chloride is impaired[9, 10] This has been confirmed by Reaser and Burch[11] who found that a normal control excreted ninety times as much radioactive sodium as did a patient with congestive cardiac failure With the retention of base, chiefly sodium, there likewise follows a retention of water, with the consequent accumulation of edema fluid which is principally water and salt Since edema fluid, as well as extracellular fluid, maintains a constant electrolyte balance with sodium chloride, there can be no loss of edema fluid without a proportionate diminution in the extracellular salt of the organism Therefore diuresis will not occur so long as the intake of sodium chloride is equal to or greater than the amount of salt excreted by the kidney

Merrill[5, 12] and others have indicated the essential role of the kidneys in the mechanism of congestive heart failure. They attribute salt retention to a low glomerular filtration rate which follows the reduction of renal blood flow, thus maintaining the kidney in its usual role as conservator of body salt Rather than an increased tubular reabsorption of water and salt as described by some,[11] these investigators further suggest that such changes in reabsorptive capacity are but slightly increased or may be entirely normal in cases of congestive heart failure and that the renal tubular work is not influenced by any unusual hormonal con

trol Under these circumstances, the primary defect lies in glomerular filtration so that the quantity of saline presented to the proximal and distal convoluted tubules is reduced far below their reabsorptive capacity

Principles of Dietary Therapy.—A considerable portion of this discussion has emphasized the role of disturbed renal function in the etiology of congestive heart failure and edema formation This concept, however, is important if we are to understand with any clarity the use of various dietary programs in the treatment of the cardiac patient A common and basic feature of the various diets presented is the continued and adequate restriction of sodium chloride

In considering the management of congestive cardiac failure, it is generally agreed that definite measures be instituted (1) to restore cardiac output to a higher level, and (2) to reduce the volume of extracellular fluid, i e , salt and water, which has accumulated in the organs and tissues of the body The first of these aims is achieved through the judicious use of digitalis or one of its derivatives,[14] along with adequate rest and sedation Such a program results in an increase of mechanical efficiency, reduction of the diastolic volume of the heart and diminution of the venous pressure The second aim of the program, to obtain a negative sodium balance, is most easily achieved with a low-sodium diet and avoidance of all medication containing the sodium ion Frequently such a program meets with failure because it is not properly carried out To be effective clinically, the daily salt intake should not exceed 1 or 2 gm , this type of diet is adequate except for vitamin content and should be supplemented with a vitamin preparation (Dayamin, Abbott, one daily, or Multicebrin, Lilly, one daily) Schroeder[10] has found that diets containing 0 5 gm sodium chloride daily are inadequate in protein content and cannot be given for prolonged periods To prevent the recurrence of failure and edema, it is essential that the patient adhere rigidly to the diet outlined for him Even a slight increase in dietary salt may precipitate the symptoms of cardiac embarrassment within four to eight days[15] Dock[16] has reported that one additional gram of sodium chloride results in the accumulation of one liter of fluid during a five day period

An additional source of error in such a program is the inadvertent administration of sodium-containing medications Among these are saline cathartics containing sodium salts, theobromine sodium acetate, employed as a diuretic, sodium bicarbonate for associated gastrointestinal complaints and sodium salicylate as an analgesic Substitutes for these types of therapy must be used if the low-sodium regimen is to succeed In those cases where sulfonamides may be essential for the proper care of the patient, Ohnysty and Wolfson[17] have reported that potassium bicarbonate is as effective as sodium bicarbonate as an alkalinizing agent, as well as possessing a definite diuretic effect They recommend that 10 gm of potassium bicarbonate be given with the initial dose of sulfonamide, followed by 2 5 gm every four hours thereafter until the medication has been discontinued Though potassium bicar-

bonate is of low toxicity, it is best to avoid its use in any case in which one suspects adrenocortical insufficiency or severe renal damage

Many patients strongly object to the tastelessness of the low-sodium diet This may be corrected to some degree by the administration of potassium chloride powder (the addition of a small amount of ammonium chloride may produce a more salty flavor), to be used in lieu of ordinary table salt Even this will not satisfy every patient, but, as Dock[16] states, " the cardiac must learn to put up with some measure of privation to retard the progress of the disease " Recently certain salt substitutes containing lithium chloride have been offered the profession and the laity to enhance the low-sodium regimen These preparations cannot be recommended because of the toxic reactions which sometimes follow their use

Protein Supplements —The necessity for protein supplements in the cardiac patient will depend upon the severity of the illness and the duration of heart failure Herrmann,[18] studying plasma protein values in one hundred edematous patients with congestive heart failure, found slight, but definitely subnormal albumin levels in all There were slight compensatory increases in globulin levels The lowest blood protein levels were discovered in patients suffering from congestive failure for many months with evidence of so-called "cardiac cirrhosis " Warren and Stead[7] were not impressed with any significant changes in blood proteins and are of the opinion that the decrease in plasma proteins following an increase in plasma volume simply serves to stimulate additional protein production Though reductions in plasma protein values may be slight in congestive failure, they should not be disregarded since hepatic function (protein synthesis) is impaired, gastrointestinal absorption may be diminished as a result of venous engorgement and, should renal damage coexist, there may be considerable albuminuria [19]

Vitamin Supplements —Vitamin requirements in heart disease with failure have not been determined with accuracy, though on a theoretical basis it would seem necessary to provide an adequate supply of all essential vitamins Sutton et al ,[20] in their series of patients with cardiac failure, found no evidence of frank thiamine deficiency and concluded that adequate doses of thiamine chloride did not influence recovery in the decompensated patient Shaffer[21] has reported a definite diuretic effect following the oral administration of ascorbic acid (vitamin C), this effect was enhanced if intravenous mercupurin were administered simultaneously He prescribed relatively large doses (500 mg daily in divided dosage) of ascorbic acid and noted the absence of diuretic effect when the preparation was given intravenously rather than by mouth The average patient, able to maintain an adequate food intake by mouth, is not likely to develop a vitamin C deficiency In other instances, parenteral vitamin preparations may be added to the intravenous feedings Supplee[22] and others have demonstrated in rats the specificity of pantothenic acid for normal balance of adrenal function Their animals grew slowly, developed exhaustion and were subject to sudden death, postmortem findings

revealed kidney, adrenal and cardiac damage with marked muscular dehydration Though these findings are the result of animal experiments, it is interesting to postulate that the same course of events might ensue in human pantothenic acid deficiency It has also been reported that frequent sudden death in cattle may follow a diet deficient in vitamin E [23] Electrocardiographic abnormalities were noted in serial tracings in one animal, and later microscopic examination of the myocardium disclosed cellular elements resembling Aschoff nodules

There is the ever-present possibility that, with the dietary restriction of sodium recommended as a cardinal feature of most present-day cardiac programs, subclinical vitamin deficiencies will result It seems logical, therefore, to supply such patients with adequate vitamin supplements

THE DIET IN CONGESTIVE FAILURE

The Karell Diet.—The standard or strict Karell diet is essentially a milk diet consisting of 200 cc feedings at four hour intervals from 8 A M to 8 P M [24] This amount will furnish

Protein	26	gm
Carbohydrate	40	gm
Fat	32	gm
Sodium chloride	1 6	gm
Water	796	cc
Total calories	552	

The above program finds its greatest usefulness in the management of the acutely ill patient in whom feeding may constitute a problem This plan entails the limitation of fluids, restriction of caloric intake and a moderately low salt intake Because of its low protein content such a diet should not be prescribed for more than six or seven days, after which time a modified diet may be instituted containing 1000 cc of milk and other simple foods such as soft boiled eggs, toast with unsalted butter and preserves and cereals with cream The addition of milk along with other sodium-containing foodstuffs may increase the total salt content of the modified diet to 2 gm which, in some patients, may delay the loss of edema fluid With the advent of more strict low sodium diets, the Karell program is now seldom prescribed

The Schemm Regimen.—This program, advocated by Schemm,[25] is based on the theory that in the cardiac patient cellular dehydration, concentration of body fluids and ultimately acidosis develop in the absence of adequate water to maintain renal function The aims of the regimen are (1) to reduce the ingestion of edema-forming materials and to encourage mobilization of retained sodium by the administration of a low sodium diet which yields a neutral or acid ash, (2) to increase the effects of normal metabolic acids by the use of acid drugs, and (3) to facilitate renal elimination of mobilized sodium and avoid cellular dehydration by the use of plain water in adequate amounts

The neutral diet recommended by Schemm is a combination of low-salt, low-sodium and acid-ash diet Each meal or feeding is carefully balanced as indicated by the outline below (after Schemm)

Limited 24 Hour Maximum	Basic Ash Foods VS.	Acid Ash foods	No limit, 24 hour Minimum
1 pint	Milk	Eggs	2
2 servings	Vegetables	Meat, fish, fowl	1 serving
2 servings	Fruits	Bread or cereals	5 slices or servings
Except		Prunes, plums, or cran berries	As desired

Precautions 1 No salt or soda in or on food
2 No prepared foods containing salt
3 No salted broth or extra juices or extra milk
4 No "vegetable" salt, no soda for "gas"

Acid drugs and diuretics to hasten the elimination of edema may not be necessary on this plan of therapy, though a mercurial diuretic such as mercupurin may be given intravenously (1 to 2 cc) if the response is slow Acid drugs are withheld if oral intake is impossible Once oral intake is established and the patient is eating the recommended neutral diet, 5 to 10 drops of dilute hydrochloric acid are added to a full glass of water to be given every hour from 7 A.M to 7 P M Should dilute hydrochloric acid not be tolerated, ammonium chloride (2 to 3 gm daily) may be substituted

The third feature of the Schemm program concerns the liberal use of plain water in amounts to compensate for that lost in the water of vaporization, urine, feces and in cellular dehydration In mild edema a minimum of 2500 to 3000 cc of water may be required, in the markedly dehydrated, edematous patient with severe kidney damage as much as 8000 to 10,000 cc may be required for a day or so Thereafter the fluid intake should be maintained at 4000 to 5000 cc daily During the initial stages of treatment, if oral intake is poor or impossible, the water may be supplied by the intravenous route, using 500 to 1000 cc of 5 per cent dextrose in distilled water from one to six times daily Schemm has observed no untoward reactions which could be attributed to the parenteral therapy If the patient is able to take fluids by mouth, a glass of water every thirty to sixty minutes should be given from early morning to 6 P.M It is often helpful to prescribe small doses of dilute hydrochloric acid, peppermint water or wine to be taken with each glass of water as a reminder to the patient of his hourly medication

Schemm has reported remarkable success with this particular plan of therapy in edematous patients with every type of cardiovascular disease as well as eclampsia, pre-eclamptic toxemias and advanced nephritis with the nephrotic syndrome[26, 27] He has not observed any deleterious effects of the high fluid intake in any patient in his series,

even in the presence of acute pulmonary edema, convulsions or papilledema In Schemm's experience all patients tolerated the high fluid intake without difficulty The question has arisen frequently as to the real desirability of forcing fluids above 3000 cc Most clinicians today believe that salt restriction is more effective in relieving cardiac edema than a high water intake [28, 29]

The Low-Sodium Diet.—Recent investigation has shown that sodium retention is a constant feature of congestive heart failure, most likely the result of renal dysfunction secondary to reduced blood flow [30, 31, 32] This is an important factor in the development of cardiac edema Each of the specific diets described above contains a minimum of sodium chloride, and this fact alone may account for considerable of their apparent success Not all patients with congestive heart failure and edema require drastic restriction of salt and, in some, the prescription of such a severe diet may be most inconvenient or often impossible to carry out The use of ammonium salts and mercurial diuretics still remain invaluable adjuncts in the treatment of congestive failure and there are no contraindications to their use in the average, well controlled cardiac patient If, however, the patient does not respond to the usual measures, a low-sodium diet containing from 1 to 2 gm of salt should be given a trial Since milk is one of the greatest sources of sodium among unprepared foods,[33] it is often desirable to substitute a sodium-free milk (Lonalac, Mead Johnson) to be used on cereals, in custards and in other foods requiring milk in their preparation It has been the experience of Wheeler[30] and others that the low-sodium program outlined below is more efficacious in the treatment of coronary and hypertensive heart disease than in cases of rheumatic heart involvement

LOW-SODIUM DIET

(After Wheeler and White)

Foods Allowed

1 Meat, boiled fish, or poultry—prepared and served without salt
2 Egg—1 daily
3 Milk—limited to 2 glasses (1 pint)
4 Vegetables—(as desired) any fresh or frozen vegetables except lima beans, prepared and served without salt
5 Fruits—(as desired) fresh, canned, stewed
6 Breads—only yeast bread prepared without salt
7 Cereals—any cooked cereal prepared without salt The only dry prepared cereals allowed are puffed rice, puffed wheat, shredded wheat and muffets
8 Potatoes and rice—prepared without salt Macaroni, spaghetti and noodles contain salt and are not to be used
9 Butter—unsalted or "washed" butter
10 Desserts—custards, junkets, and plain puddings made with milk allowance and with no added salt, jello, pies with no salt added to the crust and filling prepared with fresh or canned fruit (no meringues)
11 Beverages—tea, coffee, carbonated drinks, or fruit juices
12 Flavorings—cocoa, chocolate, caramel, maple, peppermint, lemon, orange, vanilla, maraschino cherries, cloves, cinnamon, allspice, nutmeg, ginger and coffee

13 Seasonings—pepper (black or red), curry dry mustard, mint, dill, vinegar, parsley paprika, sage, thyme, onion, garlic, pimiento, rosemary
14 Sweets—white or brown sugar, honey molasses, jellies, jams, marmalade, or preserves which do not contain sodium benzoate

Special Instructions

1 No salt is to be used in preparation of food or in cooking or is to be added to the food after it comes to the table
2 Avoid all canned foods which have salt added, such as canned meats, canned fish, vegetables, soups, tomato juice and V-8 cocktail
3 Avoid all brine-cured and smoked foods, such as bacon, ham, pickles, or smoked fish meat or sausages, and olives
4 Omit all salty foods, such as salted nuts, potato chips and buttered or salted popcorn
5 The following food accessories are also to be omitted because of their salt content meat extracts and sauces chili sauce catsup, mustard and relishes
6 Do not use any cheese clams oysters lobsters
7 Use only yeast breads prepared without salt
8 Use no foods prepared with baking soda or baking powder, such as soda crackers, biscuits, muffins cakes and cookies
9 Use only unsalted or "washed" butter Sweet butter may have salt added, so be sure to read the label before using it
10 Homemade mayonnaise may be used if prepared without salt
11 Avoid dried fruits such as figs dates, raisins apricots and prunes
12 Avoid lima beans fresh or dried
13 Sodium-containing medicines such as soda bicarbonate, soda mints tums alka seltzer and various indigestion powders should not be used Salt gargles and toothpastes containing sodium likewise are forbidden

Recipe for Salt Free Bread

6½ lbs bread flour
10 oz sugar
8 oz shortening (Primex)
4 oz yeast
2 qt water

This makes six loaves Apparently this bread takes a little longer to rise than ordinary bread

HYPERTENSIVE HEART DISEASE

Kempner[44] has reported considerable success in the treatment of hypertension utilizing a low sodium rice diet He points out that in renal disease the excretory function (formation of urine), the metabolic function (deamination of amino acids, formation of ammonia and oxidation of keto-acids), or both may be involved In those cases where the metabolic activity of the kidneys has been impaired, Kempner assumes that certain abnormal substances may appear in the blood or tissues which in the normal state are simply metabolized to harmless end products He theorizes that these intermediary metabolic substances may play a role, directly or indirectly, in the development of hypertensive cardiovascular phenomena, heart lesions or new kidney disease The hypothesis of the Kempner regimen is that, in the ordinary full diet, there may be constituents which increase the production of abnormal

toxic substances by the impaired renal cell The essentials of the rice-fruit-sugar diet, which may minimize the production of such offensive by-products of metabolism are given in the following schema

Protein	20	gm
Carbohydrate	460	gm
Fat	5	gm
Sodium	0 2	gm
Chloride	0 15	gm
Fruit juices (no water)	700–1000	cc
Total calories	2000	

Under such a dietary plan the average patient may be expected to consume 300 gm of rice daily, supplying approximately one-half the caloric requirement Any kind of rice is permitted, it is boiled or steamed in plain water or fruit juices, without salt, milk, or fat The use of salt is prohibited The liberal use of sugar (brown or white), fresh or preserved fruits is encouraged to increase the caloric intake Because of their salt content, tomato and other vegetable juices, nuts, dates and avocados should not be used in this type of diet Kempner does not favor modification of the regimen with nonleguminous vegetables, lean beef, chicken, fish or eggs since it may impede clinical improvement Iron and vitamin supplements should be prescribed daily, supplying a minimum of vitamin A, 5000 units, vitamin D, 1000 units, thiamine chloride, 5 mg , niacinamide, 25 mg , and calcium pantothenate, 2 mg Ferrous sulfate, 0 6 gm daily, should suffice

In Kempner's cases, which have included acute and chronic glomerulonephritis, chronic pyelonephritis, nephrolithiasis and hypertensive vascular disease, the diet has produced no ill effects at any time, some patients having adhered to the program for as long as thirty-two months Such therapy is frequently said to produce a rather prompt diminution of heart size, lowered serum cholesterol level, lessening of the degree of left axis deviation and reversal of inverted T-waves in Lead I Retinopathy, though improved, does not usually clear for several months No significant changes in hemoglobin, plasma protein, or chloride levels were noted in this series In 129 of the patients suffering with hypertensive vascular disease treated with the rice diet, sixty-three had signs of secondary renal involvement These cases showed the best therapeutic response The remaining sixty-six in Kempner's series provided no conclusive evidence of renal disease and demonstrated a poorer response in general to the program Since the rice diet supposedly acts by compensating renal metabolic dysfunction, one might assume that the sixty-three patients who responded so well to diet represent that type of hypertension secondary to kidney damage, while the essential hypertension of the other group may be on an extrarenal basis

SUMMARY

Recent studies have emphasized the importance of the diet prescription in heart conditions, particularly when complicated by congetives

failure In the space at our disposal an attempt has been made to review the fundamental principles underlying this aspect of the management of the cardiac patient.

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CARDIOVASCULAR MANIFESTATIONS OF BERIBERI

Based on a Study of Ten Patients

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Until about two decades ago beriberi was considered a disease of the Orient and tropics, and the syndrome of "beriberi heart" was chiefly limited to the description given by Wenckebach[1 2] who emphasized as characteristics of the clinical picture the presence of acute cardiac decompensation with an enlarged heart, particularly involving the right side, a rapid bounding pulse, "jumpy pulsus celer of increased frequency," venous engorgement, rapid circulation and pistol shot arterial sounds.

Reports from this country by Kepler,[3] Scott and Hermann,[4] Goodhart and Jolliffe,[5] Weiss and Wilkins,[6 7 8] Blankenhorn[10] and others of beriberi due to dietary deficiencies and chronic alcoholism has led to some modification of the criteria of beriberi presented by Wenckebach The studies of Weiss and Wilkins[6 7 8] and Blankenhorn[9] led them to believe that the cardiovascular manifestations of nutritional deficiency included under beriberi as observed in this country did not always lead to the rigid clinical syndrome observed by Wenckebach who described the more severe types observed in the Orient The heart was not always enlarged, the rapid circulation was not constantly present and the symptoms and signs varied considerably with the severity of the disease, furthermore, even the response to therapy was not constant These authors concluded that a diagnosis of beriberi heart disease could be made when the individual clinical characteristics of the cardiovascular changes were not specific A lack of etiology of other types of heart disease and a history of unbalanced diet was observed in all patients.

CLINICAL FEATURES OF BERIBERI HEART DISEASE OBSERVED AT THE PHILADELPHIA GENERAL HOSPITAL

Recently Blankenhorn (1945)[9] described a set of criteria for the diagnosis of beriberi heart disease which included (1) three or more months of a thiamine deficient diet, (2) signs of peripheral neuritis or pellagra, (3) enlarged heart with normal sinus rhythm, (4) insufficient evidence for other etiology, (5) dependent edema, (6) elevated venous pressure (7) nonspecific changes in the electrocardiogram, and (8) recovery with

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decrease in heart size or autopsy consistent with beriberi heart disease

Based on these criteria mentioned above we have collected ten patients with beriberi with cardiac manifestations who have been studied at the Philadelphia General Hospital Table I shows the pertinent findings in these patients

Etiology.—There were five males and five females in the series The ages ranged from 23 to 50 years, the average being 33½ years Chronic alcoholism was responsible for the poor dietary regimen in eight cases One case (No 3) was a heroin addict and ate candy and sweets for a period of five months before the onset of symptoms and signs The remaining case (No 1) ate raw starch exclusively for four years prior to admission The shortest period of poor vitamin intake, five months, was observed in a heroin addict, the longest more than ten years in a chronic alcoholic

Clinical Manifestations.—Polyneuritis was the most common sign of associated vitamin deficiency Three patients[5, 7, 9] had evidence of pellagra and polyneuritis and one (No 3) addict had a low vitamin C blood level None showed evidence of hypertensive, arteriosclerotic, rheumatic, or luetic heart disease No other etiology except beriberi was observed which could explain the heart failure

Dyspnea was observed in nine of the ten patients This varied from mild dyspnea on exertion to severe dyspnea and orthopnea at rest Six patients complained of palpitation and rapid beating of the heart In two a diagnosis of hyperthyroidism was suspected because of tachycardia, bounding pulse and high pulse pressure In both the basal metabolic rate was within normal limits

Dependent edema was the most striking sign and was present in all the patients The blood pressure was 150/110 on admission in one patient This fell to 122/84 before discharge The blood pressure of the other patients was within normal limits The cervical veins were distended and prominent in seven cases Systolic murmurs of maximal intensity over the base of the heart in the region of the pulmonary artery were observed in four patients Basal rales were present in eight patients on admission The liver was enlarged and easily palpated in five patients Edema of the lower extremities was present in every patient, in two instances the edema extended up the trunk to the thoracic cage Ascites was observed in two patients

The size of the heart, as determined by orthodiagram or x-ray, was above the predicted normal for height and weight in nine cases The shape of the heart was not characteristic, but in all roentgen studies made on admission there was evidence of pulmonary congestion and markedly increased hilar vascular markings

Electrocardiographic studies were obtained in nine patients Eight showed a normal sinus rhythm, one had paroxysms of auricular fibrillation or auricular flutter The most common abnormality was flattening or inversion of the T waves in leads I and II, with low voltage of the QRS complexes In two patients where precordial leads were taken the

TABLE I PERTINENT DATA ON TEN CASES OF BERIBERI WITH CARDIOVASCULAR MANIFESTATIONS

Case No	Color	Sex	Age	Probable Period of Dietary Deficiency	Heart Enlarged, X ray or Orthodiagram	Changes in Electrocardiogram (N.S.R.)	Dependent Edema	Signs of Other Deficiency Disease	Lack of Other Etiology	Total Serum Protein, gm. per 100 cc. / Hemoglobin / R.B.C. on Admission	Result of Vitamin Therapy
1 M R	C	F	73	8 yr	+	Normal sinus rhythm flattened $T_{1,2}$	+	Polyneuritis	+	— / 60% / 3.5 mil.	Reversion of EKG changes. Decrease in size of heart. Loss of edema. Clinical recovery
2 C R	W	M	31	4 yr	+	N.S.R., T_1 flattened T_3 inverted	+	Polyneuritis	+	6.1 gm. / 54% / 3.4 mil	Decrease in size of heart. Increase in amplitude of T wave. Improved clinically
3 A K	W	M	23	4 mo	+	N.S.R., inversion of T waves 1 & 2. QT prolonged	+	Scurvy	+	4.1 gm. / 49% / 2.06 mil	Clinical recovery with decrease in heart size and reversion of EKG to normal.
4 R. W	C	M	23	11 mo	+	Auricular flutter, auricular fibrillation, T wave flattened notched 1's	+	Polyneuritis	+	— / 74% / 2.9 mil.	Improvement of clinical signs. Died 1 year later with auricular fibrillation and auricular flutter, N.S.R. usually present.
5 A McC	W	M	32	3 yr	+	N.S.R. ST segment depressed T wave inversion of all leads	+	Polyneuritis, pellagra	+	5.9 gm / 55% / 2.84 mil	Clinical improvement. Heart smaller. Return of EKG to normal
6 R H	W	F	23	1 yr	+	N.S.R., low voltage QRS flat T's in all leads	+	Polyneuritis	+	5.0 gm. / 55% / 3.4 mil	Clinical recovery with decrease in heart size and normal EKG
7 R S	W	F	40	7 yr	+	None made	+	Pellagra, polyneuritis	+	5.5 gm / 62% / 2.9 mil	Clinical improvement with decrease in heart size.
8 C K	W	M	33	10 yr	+	N.S.R., inverted T waves in all leads	+	Polyneuritis	+	6.4 gm. / 72% / 4.0 mil	Clinical improvement. Decrease in heart size; EKG returned to normal
9 F D	W	M	60	3 yr	+	N.S.R., low voltage QRS and T's	+	Polyneuritis, pellagra	+	4.9 gm / 55% / 2.5 mil	Clinical improvement. Heart smaller in size and EKG showed increased voltage.
10 E. S	W	F	35	15 mo	—	N.S.R. prolonged QT interval	+	Polyneuritis	+	5.0 gm / 64% / 2.6 mil	Clinical improvement, shortening of QT interval

Reported by Kepler (1925)[9]

T waves were also inverted Prolongation of the Q-T interval was observed in two patients These changes returned to normal following improvement in the clinical state of the patient

The venous pressure was determined in six cases, in two this was within normal limits and in four it was elevated, the highest venous pressure obtained was 240 mm of water (No 6)

The circulation time was determined in five instances, the longest arm to tongue time was 14 seconds, the shortest 7 seconds One patient's circulation time was 10 seconds and two were 12 seconds In all instances the pulse was rapid, bounding and collapsing in nature, suggestive of a Corrigan pulse

Laboratory Studies.—In eight patients where serum proteins were obtained a hypoproteinemia was present, in six of these patients it was marked With clinical improvement the serum proteins returned to normal A secondary anemia was present in all of the patients on admission

Response to Treatment.—The response to treatment was variable All of the patients of this series showed a rapid clinical improvement The dyspnea and edema decreased within twenty-four to forty-eight hours The heart gradually decreased in size and attained its smallest diameter within fourteen to twenty-one days following admission, the decrease in heart size ranged from 1 5 cm to 3 5 cm in the transverse diameter The electrocardiogram returned to normal within fourteen to twenty-eight days in most cases It is interesting to note that three patients returned to the hospital within periods of one to three years with far advanced pulmonary tuberculosis, and a fourth patient (No 10) is now back in the hospital with suspicious tuberculous lesions in the hilar areas.

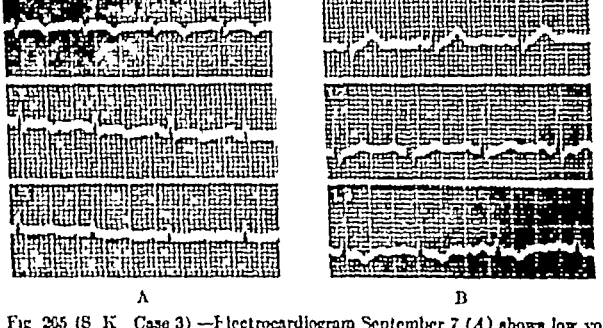
CASE REPORTS

CASE 3 —S K, *a white male 23 years of age*, was admitted to the Medical Ward on September 8, 1938, with a provisional diagnosis of cardiac decompensation and acute glomerulonephritis He presented the following history In March, 1938, discouraged by his inability to obtain work he began taking daily injections of heroin "by the main track" (intravenously) About August 1 he was arrested for petty thievery and sent to jail and twelve days later he was admitted to the hospital with the present illness Since the onset of the heroin addiction in March, 1938, he had eaten only candy and sweets He had been in his usual state of fair health until eleven days before admission to the medical ward when he awakened in his cell and found his legs swollen The swelling increased and his weight increased from 140 to 175 pounds in the eleven days prior to admission He stated that he had never had "smoky" or bloody urine, although recently the urine was dark brown

Physical examination showed a large, pasty and puffy faced young white male, propped up in bed, evidently quite ill The cervical veins were distended The blood pressure was 150/110 The chest showed crepitant rales and bronchovesicular breathing at both bases The heart was enlarged, the rhythm was regular, the heart sounds were loud and forceful, and no murmurs were heard The abdomen was distended and tense and free fluid was present The legs were

markedly edematous, the edema extending up the back to the level of the lower ribs The reflexes were normal and no abnormal responses were obtained The provisional diagnosis was the nephrotic stage of acute glomerulonephritis

At this time, the history was obtained from the patient who stated that since March, 1938, he had eaten only candy and sweets Laboratory studies showed the urine to be normal, urea nitrogen was 25 mg per 100 cc , the total protein was 4 1 gm per 100 cc , albumin, 2.8, globulin 1.3, the vitamin C in the blood serum was found to be 0 40 mg per 100 cc , a subclinical level of scurvy The electrocardiogram (Fig 205) showed markedly inverted T waves in leads I and II, and on the basis of the initial history given, the possibility of pericarditis or possibly uremia was considered The x ray of the chest showed the heart to be moderately enlarged with congestion in the inner zones



A B

Fig 205 (S K Case 3) —Electrocardiogram September 7 (*A*) shows low voltage of the QRS complexes, marked inversion of the T waves in leads I and II and a prolonged Q T interval Electrocardiogram taken November 20 (*B*) has returned to within normal limits

Because of the failure to substantiate a diagnosis of the nephrotic stage of glomerulonephritis and because the patient gave a history that for five months preceding admission he had eaten only candy and sweets, the diagnosis was changed to beriberi, and treatment instituted for this condition The patient was started on a high protein diet, brewers' yeast, cevitamic acid, ferrous sulfate and cod liver oil. On September 19, eleven days after admission, the edema had disappeared, the blood protein level was 5.2 gm per 100 cc , the blood pressure was 122/84 the signs of congestion in the chest had disappeared the heart was smaller but the changes in the electrocardiogram persisted. On October 3 following a chill and a rise in temperature, the spleen became palpable and a blood smear was positive for the parasite of malaria He was treated for the malaria and made a routine recovery At the time of discharge November 22, his condition was considerably improved, the edema had disappeared and the electrocardiogram had returned to normal (Fig 206) The total serum proteins were now 7.2 gm per 100 cc

Comment —This patient is an example of "wet beriberi" with a relatively acute onset of myocardial failure It is interesting to note that

although all the edema had disappeared eleven days after admission, the total serum proteins were still quite low (5 2 gm per 100 cc) The changes in the electrocardiogram were marked and striking and the return to normal lagged behind clinical recovery and decrease in heart size

CASE 8 —C K , a 39 year old white male, was first admitted to the alcoholic ward of the Philadelphia General Hospital in March 1943 at the age of 34 The patient stated that since the age of 19 he drank a pint or more of whiskey daily Between the first admission in 1943 and the ones we are reporting he had ten admissions to the alcoholic ward On November 6, 1948, he was readmitted to the alcoholic ward

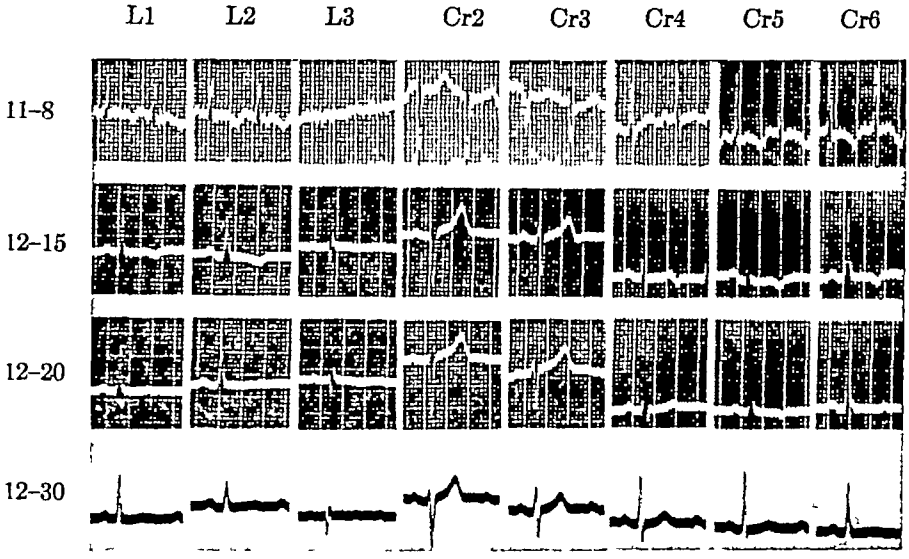


Fig 266 (C K , Case 8) —Electrocardiogram November 8 (tenth admission shows inversion of the T waves in the limb leads and the left precordial leads December 15 (eleventh admission) shows little change except that the rate is slower December 20 shows the T waves to be flattened in the limb leads and inverted in leads Cr_5 and Cr_6 December 30, the T waves are upright although of diminished amplitude

Physical examination showed a well nourished, florid white male, somewhat dyspneic, not acutely ill The neck veins were visible and distended The blood pressure was 120/65, the heart was slightly enlarged to percussion, the heart sounds were of fair tone, no murmurs were heard The liver was palpable 4 cm below the costal margin The ankles were edematous, the edema extending up to the knees The venous pressure was 120 mm of water, the arm to tongue circulation time (5 cc of 10 per cent strontium bromide) was 14 seconds The serum proteins were 6 2 gm per 100 cc An orthodiagram (Fig 267) showed the transverse diameter of the heart to be 15 7 cm , 18 per cent above the predicted figure for his height and weight The electrocardiogram (Fig 266) taken November 8, 1948, showed a simple tachycardia with a rate of 140 per minute, and inverted T waves in leads I, II, Cr_5 and Cr_6 The patient was placed on a high carbohydrate, high protein, low fat diet and given thiamine intravenously and intra-

muscularly As the edema disappeared, evidence of polyneuritis was noted with shooting pains in the legs and paresthesias The improvement in the electrocardiogram can be seen in Figure 206 Despite the clinical improvement the pulse was rapid and collapsing in type (Fig 208) At the time of discharge the transverse diameter of the heart was 13 5 cm , (Fig 207) a decrease of 2 2 cm , and within normal limits with regard to predicted figures for height and weight

Comment—The long alcoholic history, the cardiac enlargement and evidence of heart failure without obvious cause, the polyneuritis, and the improvement following adequate vitamin therapy suggested beriberi

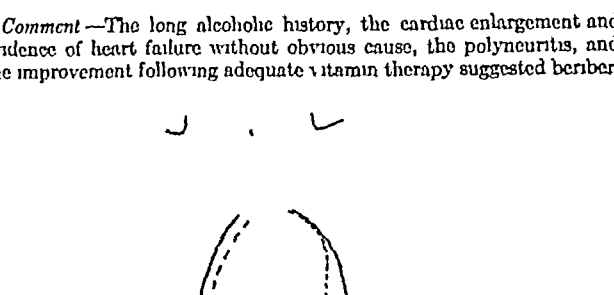


Fig 207 (C K , Case 8) Solid line—orthodiagram December 15 Dotted line—orthodiagram December 30, after treatment

as the underlying cause of these findings. The cardiac enlargement and the electrocardiographic changes returned to normal with improvement of the patient

Case 10—E S , a 35 year old white female, was admitted to the medical ward on September 30, 1918 complaining of painful, swollen legs abdominal pain and numbness of the hands She gave a history of being perfectly well with the exception of a ruptured ectopic pregnancy in 1930, until one and a half years ago At that time because of marital difficulties resulting in divorce, she went on a "boozo spree" which continued until the time of admission She drank between 1 and 2 pints of whiskey daily and ate very little Her appetite for food failed rapidly Three months before admission she noticed that her abdomen and legs were swollen At about this time she experienced knifelike pains that radiated from her legs to the thighs Two weeks before admission she noted numb-

ness of her hands and a constant dull ache in the legs and feet She often fell down when walking because of the excruciating pain in the extremities She finally became bedridden and was unable attend to herself One and one-half years ago she weighed 145 pounds, on admission her weight was only 89 pounds

Examination revealed a very thin, pallid woman who was quite dyspneic There was evidence of marked weight loss The neck veins were distended and there was marked pulsation of the vessels in the neck The blood pressure was 120/60 There was no enlargement of the heart to percussion No thrills were palpable and no murmurs were heard The heart sounds were fair in quality and a gallop rhythm was present The liver was palpable 3 cm below the costal

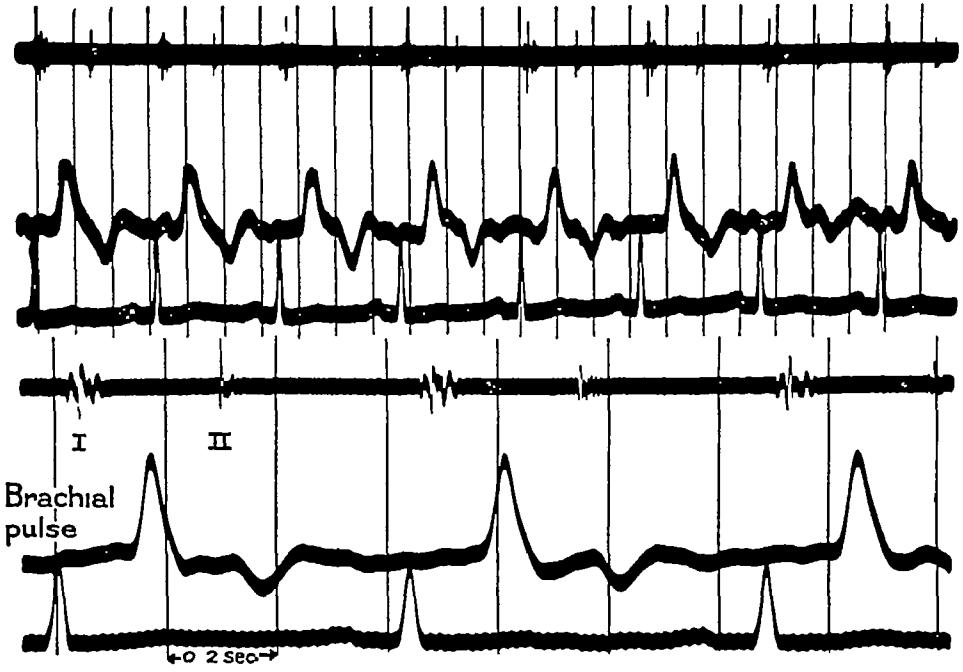


Fig 268 (C K , Case 8) Simultaneous phonocardiogram (5th left intercostal space, mid-clavicular line), pulse tracing (brachial artery) and electrocardiogram The top record was made at the normal speed of 25 mm per second, the bottom record at 75 mm per second The pulse is collapsing in the type suggestive of aortic insufficiency, the beginning of the upstroke to the peak of the primary wave 0 05 second and 0 11 seconds to the predicrotic summit (normal 0 23 second) The phonocardiogram shows no evidence of a diastolic murmur

margin, it was firm in consistency and no nodularity was noted Edema of the legs was noted and extended up the thighs to the lower abdomen Scattered areas of anesthesia and hypesthesia were noted, covering both legs and the lower abdominal wall X-ray of the chest showed the heart to be normal in size, with marked congestion of the inner zones and prominent bronchovascular markings An electrocardiogram showed a prolonged Q-T interval with some flattening of the T waves in leads I and Cr_6 The venous pressure was 140 mm of water The circulation time arm to tongue (5 cc of 10 per cent strontium bromide) was seven seconds The total serum proteins were 5 0 gm per 100 cc , albumin 2 8, globulin 2 2, hemoglobin 64 per cent and the red blood count 2,400,000

The patient was given 50 mg of thiamine chloride intravenously and 75 mg

intramuscularly daily In addition she was given nine tablets of brewers' yeast, niacin, 200 mg. intravenously, cevitamic acid 100 mg intravenously and choline hydrochloride 30 grains per day Within five days there was a remarkable clinical improvement Her dyspnea and edema disappeared and she was up and about in the ward assisting the nurses Despite the clinical improvement, a tachycardia persisted and an electrocardiogram on October 17 showed little improvement in the amplitude of the T waves, but the Q T interval was shorter Tracings of the right femoral pulse (Fig 269) show a rapid collapsing type of pulse which is further evidence of peripheral vasodilatation She was discharged on October 22 at her own request She was instructed to return to the outpatient medical clinic and to continue her vitamin intake orally

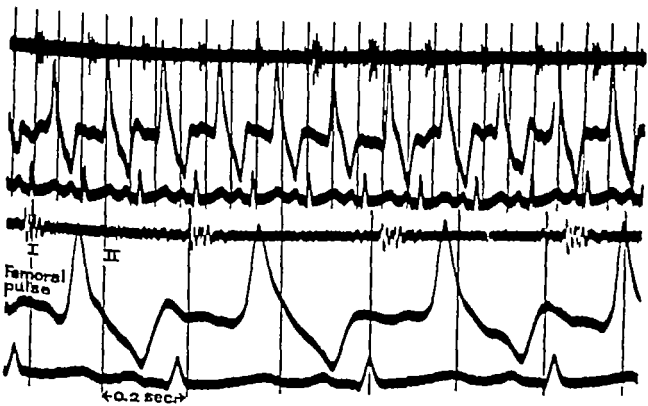


Fig 269 (E S Case 10) —Simultaneous phonocardiogram 5th left intercostal space, midclavicular line, pulse tracing (femoral artery at the groin), and electrocardiogram The pulse wave is collapsing in type, beginning of upstroke to peak of primary wave 0 04 second beginning of upstroke to predicrotic summit 0 03 second

Comment —This case represents one of "wet beriberi," with evidence of an advanced grade of myocardial failure This patient manifested the rapid collapsing type of pulse and the rapid circulation time characteristic of this condition The loss of edema and rapid clinical improvement followed specific therapy

CLINICAL FEATURES OF BERIBERI WITH CARDIAC MANIFESTATIONS

The essential features pertaining to the heart in patients with beriberi, most of which were illustrated by the patients in our series, are summarized below

Etiology —The primary etiologic factor is thiamine deficiency Multiple nutritional deficiencies are a factor in the development of beriberi with cardiovascular manifestations However, that thiamine de

is the primary factor in this condition is demonstrated by the following observations: (1) the thiamine content of the diet is low while the caloric intake is high; (2) thiamine therapy results in improvement and disappearance of the characteristic symptoms and signs, (3) electrocardiographic changes similar to those observed in this condition can be induced by giving a thiamine-deficient diet to healthy persons,[10] and (4) similar electrocardiographic changes to those described above and congestive failure have been induced in animals kept on a thiamine-deficient diet.[7] In the Orient the diet of polished rice, which is rich in calories but poor in thiamine, predisposes to beriberi. In the Occident the great majority of patients who develop beriberi heart disease give a history of excessive intake of alcohol plus a poor diet. The length of time necessary to produce the syndrome of beriberi heart disease varies with such factors as the degree of hypovitaminosis, the amount of physical activity of the patient and the presence or absence of a complicating disease. Thus, in a patient with mild manifestations of polyneuritis who is apt to continue his muscular work, a severe type of congestive failure may develop relatively rapidly.

Symptoms and Signs.—The symptoms and signs vary considerably with the severity of the disease. In general the symptoms are those of cardiac decompensation and myocardial failure due to any other cause. Peripheral edema may be slight or extensive and is frequently generalized. The patient often shows marked distress with severe dyspnea and orthopnea. The veins are distended and prominent with marked pulsations of the underlying carotids. The heart rate is usually rapid. This is in contrast to the bradycardia described by Keys[11] in cases of undernutrition and starvation with cardiovascular manifestations.

On palpation a forceful cardiac impulse is observed. The heart is enlarged both to the right and left. A systolic murmur may be heard which is characterized by its variability in intensity and quality. A gallop rhythm, protodiastolic or presystolic, is frequently present. The blood pressure readings are not characteristically altered, the systolic pressure may be elevated but is usually within normal limits. In a severe case the pulse pressure is elevated, prominent arterial pulsations are present and pistol shot sounds may be heard over the large arteries, in mild cases the peripheral arterial pulsations are normal.

Roentgen study shows the cardiac silhouette to be enlarged to the right as well as to the left, with no characteristic shape. The hilar shadows and bronchovascular markings are often markedly increased and prominent.

Changes in the electrocardiogram are not specific. A normal sinus rhythm is usually present. The most frequent change is low voltage of the ventricular complexes. The T waves may be inverted in the limb and precordial leads, the Q-T interval may be prolonged, bundle branch block[12] may occasionally be present. The reversion of the electrocardiogram to normal may lag behind clinical recovery.

Hypoproteinemia is frequently found and may be quite severe in degree An associated secondary anemia, moderate to mild, is the rule

The syndrome of beriberi heart disease is a combination of overactivity and failure of the heart It is similar to the clinical picture observed in thyrotoxicosis and arteriovenous aneurysm where there is a "high" output failure" as described by McMichael[13] Burwell and Dexter[14] reported studies of the circulatory dynamics as determined by means of right heart catheterization in a case of beriberi heart disease Studies made before treatment was begun showed the cyanide time to be 13 seconds, the venous pressure 300 mm of water, the pressure in the pulmonary artery 64/30 mm Hg, the pressure in the right ventricle 65/17 mm Hg, and the cardiac output to be 11 8 liters per minute The patient was given 10 mg of thiamine hydrochloride every six hours Improvement was apparent in a few days After thirty days the patient was so much improved that he was catheterized again with the following findings venous pressure 90 mm of water, pulmonary artery pressure 32/14 mm Hg, right ventricular pressure 32/0 mm Hg, and cardiac output 5.3 liters per minute, a fall of 54 per cent The pathologic physiology underlying the increased velocity of the blood, the collapsing type of pulse, the right sided heart failure and the increased cardiac output is dilatation of the peripheral arteriolar system The numerous dilated arterioles act in the same manner as an arteriovenous fistula, in that there is no capillary bed between the arterial and venous circulation

Differential Diagnosis —The essential features of beriberi heart disease are the presence of myocardial failure with rapid circulation in a relatively young person associated with the history of a thiamine-deficient diet and lack of etiology of other types of heart disease In the differential diagnosis one must consider thyrotoxicosis, arteriovenous aneurysm, amyloidosis, glycogen storage disease (von Gierke), cirrhosis of the liver, glomerulonephritis, lupus erythematosus, scleroderma, Boeck's sarcoid, periarteritis nodosa and idiopathic postpartum myocardial failure

Pathology —The pathologic picture varies with the duration and severity of the disease Wenckebach,[2] who observed severe grades of the disease, reports enormous dilatation of the right heart, engorged veins, hydropic degeneration of the heart muscle and fibrosis of the myocardium The weight of the heart may be normal but with chronic deficiency the heart is usually hypertrophied Histologic study usually shows interstitial edema and hydropic degeneration of the myocardial fibers The interstitial edema is composed of collagenous material In some instances[11, 16] cardiac and mural thrombi, which give rise to embolic phenomena, have been observed Figure 270[17] shows a section of myocardium from a white female, 32 years of age, who had severe diabetes accompanied by avitaminosis A and B_1 At autopsy, the microscopic examination of the heart showed "the muscle cells to be small, a large number of them vacuolated (hydropic degeneration), and there was

fragmentation of the muscle fibers with longitudinal separation of the bundles due to edema "

Treatment.—Bed rest alone will result in improvement in mild cases, and dependent edema will diminish The specific treatment consists in parenteral administration of thiamine hydrochloride in doses of 10 to 30 mg three times a day In severe cases a daily intravenous dose of 50 to 100 mg may be needed Although thiamine and vitamin concentrates are effective orally, it is advisable to give the drug subcutaneously or

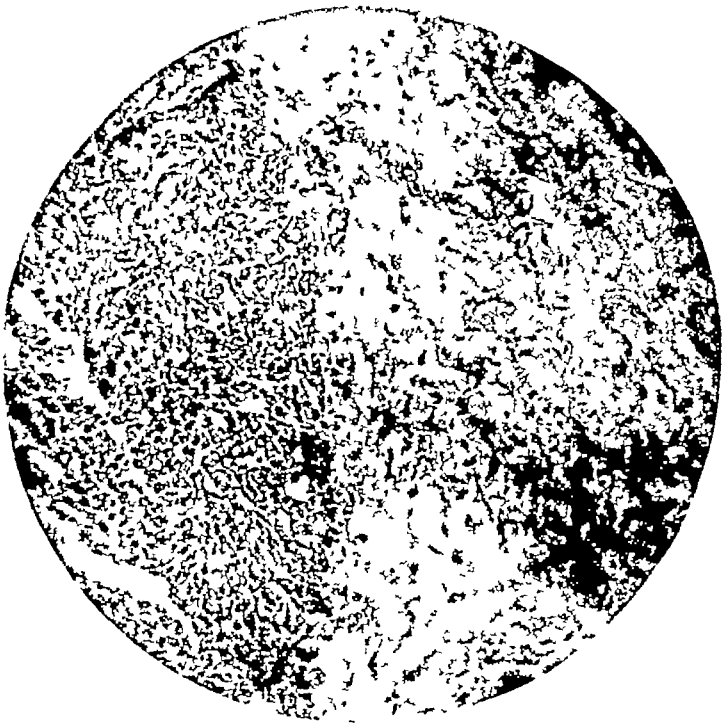


Fig 270 —Edema of pericardium, hydropic degeneration and fragmentation of heart muscle (Wohl, M G , J A M A , Vol 87)

intravenously because gastrointestinal or liver disorders may interfere with the utilization of the vitamin Thus Alleman and Stollerman[18] found that when parenteral therapy was discontinued and the patient placed on oral vitamin therapy, there was a recurrence of symptoms and signs

Digitalis, mercurial diuretics and restriction of salt intake are indicated in markedly edematous patients The improvement with digitalis is not a point against a diagnosis of beriberi heart disease and as Blankenhorn et al [19] state, "digitalis would be expected to help in a heart where failure is due to loss of tone and contractility "

Since patients with beriberi have multiple deficiencies, simultaneous treatment must be given for pellagra with nicotinic acid, for hemorrhagic

tendencies with ascorbic acid and vitamin K and the treatment of anemia with iron and liver extract

The response to treatment varies As a rule, the signs of congestive failure disappear early, reduction in size of the heart and reversion to normal of changes in the electrocardiogram occur later and in a more gradual manner The fact that the myocardium in beriberi can develop hypertrophy, hydropic degeneration and deposition of interstitial collagen demonstrates that a prolonged thiamine deficiency may change from an easily reversible to a slowly reversible or irreversible state

SUMMARY

This report is a discussion of the pertinent findings of ten patients with beriberi who presented cardiovascular manifestations The clinical findings and subsequent course of three patients are reported in detail The essential features of this syndrome, including the underlying etiology, clinical manifestations, diagnostic features, laboratory studies and treatment, are discussed

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THE NUTRITIONAL ASPECTS OF LIVER INJURY

PAUL GYÖRGY, M.D *

The recognition and proper appreciation of nutritional factors in the prevention and treatment of several forms of hepatic injury resulted from the merger of both clinical and experimental observations

Clinical experience suggested that the often recurrent etiologic factor, i e chronic alcoholism, in Laënnec's cirrhosis might produce a condition of deep-seated nutritional deficiency In further consequence, "alcoholic" cirrhosis should be considered as basically similar to "alcoholic" beriberi or pellagra, amenable to proper dietary treatment In 1937, Patek[1] in a preliminary statement reported on favorable therapeutic results obtained in thirteen patients, kept for one year on a diet rich in protein and in vitamin B complex These studies were further extended, and therapeutic results covering fifty four patients were published in 1941 by Patek and Post,[2] fully confirming their previous preliminary observations

Simultaneously with these empirical clinical studies, experimental investigations were carried out in several laboratories on the production and prevention of hepatic injury

It may be stated without fear of contradiction that modern medical progress is based to a very large extent on animal experiments. Conclusions gained in such animal experiments have proved to be applicable with a high "batting average" to equivalent conditions in human pathology As a matter of fact, confirmation by experimentation on animals puts clinical observations often on a much more respected and generally acceptable foundation Animal experiments may be better supervised, organized, and controlled than analogous clinical investigations, thus they permit a more exact, almost mathematical evaluation, in contrast to clinical studies with all their inherent difficulties In logical consequence, in the specific case of hepatic injury, conclusions reached in animal experiments should permit a more direct analysis of the underlying etiologic and pathogenetic factors, and should also aid materially in the management of the corresponding conditions in man In the following, we shall confine our remarks largely to the discussion of experimental hepatic injury, but will point out the interrelation with the corresponding clinical entities

DIETARY FACTORS IN THE PRODUCTION OF EXPERIMENTAL HEPATIC INJURY

From a pathologic point of view, necrosis and cirrhosis are the characteristic manifestations of injury to the hepatic parenchyma Fat in-

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filtration per se is not specific enough, and often too transient, without concomitant manifestations of tissue reaction, to be considered in itself as a truly pathological condition of the liver

Three outstanding results characterize the latest developments in the experimental approach to diseases of the liver, namely (1) the recognition of purely nutritional factors as important determining causes of hepatic injury, (2) the prevention, arrest and even possible reversal of this pathologic process simply by proper change in the composition of the experimental diet, and (3) the interrelation between dietary, endocrine and genetic factors in the pathogenesis of hepatic injury

In the past, experimental hepatic injury was produced through exposure of the living animal to various hepatotoxic agents From these experimental studies, which in general tally well with clinical observations, it was concluded that in every instance in which the prolonged or repeated "action of an agent has resulted in some degree of cirrhosis, the acute effects have been degeneration and necrosis of hepatic cells "[3] From this point of view, necrosis and cirrhosis are the acute and chronic forms of hepatic injury, often in response to the same etiologic agent The response of the hepatic tissue to insults of various kinds manifests itself in necrosis when the insult is overwhelming, or when the resistance of the hepatic parenchyma is reduced below the norm, whereas continuous or repeated exposure to the same agent given in doses which are in general below the necrogenic level results in cirrhosis When cirrhosis follows interrupted, repeated exposures of hepatic tissue to a noxious agent, it may be inferred that the injurious effect is achieved by proper timing of the insults which precluded the complete repair of the hepatic parenchyma between consecutive exposures, and reduced the normally high regenerative power of hepatic parenchyma

On the basis of these toxicologic studies, necrosis and cirrhosis were generally looked upon as only quantitatively different manifestations of hepatic injury The recent recognition[4, 5] of physiologic, dietary conditions as predisposing factors in hepatic injury necessitated a revision of this strictly unitarian point of view It has been shown that the etiologic dietary factors which determine the development of acute necrosis are in many respects not only different, but appear to be diametrically opposed to those instrumental in the experimental production of diffuse fibrosis[5, 6]

The most commonly used diet for the production of hepatic injury is characterized by a low content of protein in the form of casein and by a high content of fat In rats kept for a prolonged period on such a diet, hepatic injury, either in form of acute massive or zonal necrosis, or of diffuse fibrosis, is a regular occurrence The low protein intake was first considered the primary etiologic factor It has long been known that dietary protein may neutralize to some extent the toxic effect of various hepatotoxins[3, 6] Furthermore, in this connection it is of interest that a diet low in protein promotes extensive fat infiltration of the liver, which may be prevented by the addition of casein As has been shown by Best

and his associates, and later by many others,[7] choline and, to a lesser extent, betaine exhibit similar "lipotropic" activity The lipotropic activity of casein is generally believed to be in direct proportion to its content of methionine and to the presence of choline in the diet, but is adversely influenced by cystine either in form of the free amino acid or of a protein high in cystine and relatively low in methionine, such as peanut protein

It was surprising to find[5 8 9] that supplements of choline or liver extract to the experimental (low protein) diet would prevent cirrhosis but were without influence on, or would even promote, acute diffuse necrosis Conversely, cystine given as a supplement to the experimental diet exerted a remarkable protective effect on the development of necrosis, but seemed to enhance the production of hepatic fibrosis Methionine, on the other hand, prevented both acute diffuse necrosis and cirrhosis. In the light of these observations it has been claimed[5 9] that acute massive or zonal necrosis is due to deficiency of sulfur-containing amino acids, especially cystine, whereas diffuse hepatic fibrosis was considered to be the final outcome of mechanical obstruction of normal blood supply following chronic fat infiltration,[8 10 11] which in itself is caused by lack of lipotropic substances, i.e , choline and its precursors, including methionine (protein)

Several more recent observations seem to be at variance with this concept These discrepancies regarding the etiology of the two specific forms of hepatic injury, necrosis and cirrhosis, may best be discussed separately

Necrosis.—Acute necrosis, when produced on a ration low in casein, presents itself mainly in the form of acute zonal (central and midzonal) necrosis appearing in many lobules and frequently in all lobes In some cases it becomes massive and complete, involving the total hepatic parenchyma of many lobules, or even of an entire lobe

The gross and microscopic features of acute necrosis of the liver in rats produced by purely dietary means are analogous to those seen in acute necrosis, often still called "acute yellow atrophy" of the liver in man, occurring in acute hepatitis or under the influence of hepatotoxins such as carbon tetrachloride Condensation fibrosis or its equivalent, postnecrotic scarring, represents the healing stage of massive necrosis With the addition of choline to the experimental ration low in casein, cirrhosis may be completely prevented, but the incidence of necrosis, although accelerated and intensified, increased in our experience only slightly, and never reached more than about 40 per cent The irregular occurrence of massive necrosis in rats fed a diet low in casein was claimed[5] to be due to the quality of the casein which, when given in a small amount supplied methionine (and cystine) not too far below the prophylactically effective level

By substituting yeast for casein the intake of sulfur-containing amino acids may be further lowered In rats fed rations with yeast as the sole source of protein the incidence of massive necrosis was reported[4 12 13] to have increased considerably and to have reached 80 per cent and more in various experimental groups This necrosis seen in rats which were fed the experimental yeast diet

was usually very widespread, truly massive and intensely hemorrhagic, involving mainly the left half of the liver [5, 12] The development of hepatic necrosis was again completely suppressed by prophylactic supplements of cystine[5, 6, 12, 13] or methionine [5] Thus, the results obtained seemed to confirm the thesis that necrosis is due to deficiency of sulfur-containing amino acids and seemed to give a satisfactory explanation for the relatively low incidence of massive necrosis in rats fed rations with the not completely suitable casein as protein

However, the identification of dietetic massive necrosis as simple cystine deficiency leaves several recent observations unexplained For instance, attempts to produce massive hepatic necrosis were unsuccessful in several laboratories, with yeast rations[14] or with any other diet forms [15, 16] These negative results were recorded in spite of the fact that in all the rations used the intake of sulfur-containing amino acids was kept at a very low level, and apparently within the same limit as in the original yeast experiments with their high incidence of massive hepatic necrosis Addition of tocopherol to rations containing lard, or substitution of vegetable fat, rich in tocopherol, for lard, suppressed almost completely the development of massive hepatic necrosis [17] The inadvertent inclusion of tocopherol in the experimental diet may also explain the failure to produce hepatic necrosis in rats kept on diet forms which, without supplements of tocopherol, have proved to be conducive to the production of hepatic necrosis The production of hepatic necrosis is significantly delayed in rats taken from a stock which received a diet rich in tocopherol [18]

Thus tocopherol emerges as an important additional protective dietetic factor in the etiology of hepatic necrosis With regard to the development of massive hepatic necrosis, tocopherol may compensate for the absence of cystine and/or methionine, and vice versa

At present, it is by no means certain that with the two dietary factors named, i e , sulfur-containing amino acids (cystine, methionine) and vitamin E, the etiology of massive hepatic necrosis would be completely defined In this connection it should be noted that substitution of one kind of yeast for another may materially influence the development of hepatic necrosis, as observed in rats fed the usual necrogenic yeast ration In our own experience a special, active dry British yeast promoted hepatic necrosis, whereas the same experimental ration with a particular inactive American yeast suppressed hepatic necrosis It is very unlikely that this difference in effect should be due to differences in the content of cystine (and methionine) or tocopherol in the two types of yeast in question

In spite of these and similar unexplained findings, it cannot be denied that the sulfur-containing amino acids and vitamin E occupy an important and probably key position in the etiology of massive necrosis The interchangeability of sulfur-containing amino acids (cystine, methionine) and vitamin E as leading etiologic factors makes it difficult to accept pure deficiency as the basis of acute diffuse hepatic necrosis Furthermore, cystine when given in excessive doses[19–21] and often even not too greatly[22] in excess of the physiological norm, will not only not prevent, but, in fact, will promote the production of massive hepatic necrosis Methionine and cystine have been known for long as detoxifying agents in counteracting the noxious effect of massive hepatotoxins and

related poisons[4, 6] Recently, similar observations were reported with regard to the effect of vitamin E in the particular case of carbon tetrachloride poisoning[22] In rats kept on the usual low-casein, high-fat diet and supplemented with the carcinogenic dye, N-N-dimethylaminoazobenzene (butter yellow), massive necrosis reached a much higher incidence than in control groups fed the same diet without butter yellow Nevertheless, in both groups, supplements of cystine or tocopherol prevented the development of massive necrosis equally well[17] This may indicate that cystine and tocopherol neutralized first the effect of the exogenous poison, butter yellow, and simultaneously also that of some unrecognized "cryptogenic" metabolic poison Massive necrosis caused by large doses of cystine should also be considered as a toxic manifestation, perhaps initiated by the disturbed normal ratio of cystine to choline[4] in the diet and in the body In this connection one should recall the enhancing effect of choline and choline-like substances (liver extract) on the production of massive hepatic necrosis in rats fed a ration low in cystine and methionine

The phenomenon of acute hepatic necrosis provides an impressive illustration of the difficulty encountered in distinguishing between mechanisms based primarily on deficiency or intoxication These mechanisms may be thoroughly interwoven, as in the case of dietary hepatic necrosis, and do not permit a distinct separation of factors relative to deficiency or to intoxication

In man, acute necrosis—as far as it can be determined in a given case—follows toxic insults (infection, poison, or metabolic toxemia, such as eclampsia or erythroblastosis) and not a conspicuous dietary deficiency Thus, the above considerations may help to establish a closer relation between clinical and experimental hepatic necrosis, with practical implications which are self-evident but should be discussed later in detail

Cirrhosis —In contradistinction to the difficulties encountered by several research workers in their effort to produce so-called dietary hepatic necrosis in rats, unanimity was early established as to the ease with which diffuse hepatic fibrosis develops in rats, when kept on a diet low in "lipotropic" factors In short term experiments the absence of lipotropic factors manifests itself by fatty infiltration of the liver Prolonged feeding with a diet free from, or low in, lipotropic factors leads to cirrhosis This sequence should, however, not be regarded as proof for a direct relation between fat infiltration of the liver and cirrhosis Both conditions may occur only coincidentally, and, conversely, fatty infiltration of the liver may exist in animals and also in man for a prolonged period without the concurrent existence or production of cirrhosis

The simplest semisynthetic diet, which in rats will produce cirrhosis in 100 to 150 days, should have a low casein content, should be high in fat and be supplemented with the usual water soluble and fat-soluble vitamins. Even larger amounts of protein may be substituted for casein, provided the protein, for example, peanut meal, is poor in methionine

In addition to the lipotropic factors there are also anti lipotropic fac

tors, such as fat and cystine Among the fats, lard seems to promote the development of cirrhosis, compared with the effect of vegetable shortenings Cod liver oil is especially injurious The obvious attempt to seek a direct correlation between this noxious effect of lard and cod liver oil, and their low content of tocopherol, is refuted by the observation that supplements of tocopherol, even in very large doses, leave the development of diffuse fibrosis unaltered in rats receiving lard and cod liver oil in their experimental rations On the other hand, no link is visible between the specific cirrhosis-producing effect of fats like lard and cod liver oil, and the lipotropic (choline and its precursors) or the antilipotropic (cystine) factors

The gross and microscopic pictures of experimental dietary cirrhosis in rats bear a close resemblance to those seen in nonexperimental, so-called Laënnec cirrhosis in man However, there are a few discrepancies or distinctive features which require further analysis and discussion

One distinctive feature of dietary cirrhosis is the presence of an acid-fast, golden-brown fluorescent pigment, called "*ceroid*"[4 24–28] This pigment appears to be closely related, but probably not completely analogous with the pigment seen in the uterus, ovary and muscles in vitamin E deficiency in animals,[29] or with the very similar "wear and tear" pigment seen in the regressing corpus luteum in the ovary, or in the regressing Leydig cells of the testicle and in the reticular layer of the adrenal gland [28] However, its identical counterpart has not yet been found in human liver, either in ordinary cirrhosis or in hemochromatosis [28] Tocopherol, even when given in excessively large doses (30 mg daily), will not prevent the formation of ceroid, and will reduce only slightly its total quantity as found in the cirrhotic livers of the experimental animals [6] Experimental cirrhosis, without ceroid, may be produced provided that cod liver oil and, to a lesser degree, all other sources of unsaturated fatty acids (in large concentration), are eliminated from the experimental diet [6] Thus, ceroid is not an essential and important feature of experimental cirrhosis Its absence in the cirrhotic liver of man is not surprising, neither cod liver oil nor unsaturated fat in large amount is a part of a normal dietary for man

A further discrepancy between experimental cirrhosis in rats and Laënnec's cirrhosis in man refers to the topographical distribution of the hepatic fibrosis The view is generally held that Laënnec's cirrhosis in man is based mainly on portal fibrosis, and the destruction of the normal architecture of the liver in this condition must start by fibrous proliferation from the portal space Careful analysis of the histological pictures observed in various stages of progression revealed the interesting finding that in experimental dietetic cirrhosis of the liver, in rats, the fibrotic changes seem to begin not in the portal spaces but have their origin as first recognized by Ashburn and his associates[30] close to the central vein,[6 31] with a distribution of the connective tissue around the central vein, which is different from that of so-called central cardiac cirrhosis In later stages, the fibrous bands may be both portal and nonportal in distribution

The nonportal distribution of fibrosis in experimental dietary cirrhosis has an important bearing on its pathogenesis This situation could be interpreted as the direct result of chronic fat infiltration, with mechanical obstruction of the intralobular sinusoids and resulting anoxia which should affect primarily the nonportal, and especially the central, parts of the lobules The fact, however,

that fat infiltration of maximum intensity may exist in the liver for a long period, without concomitant appearance of fibrosis, and the development of pronounced cirrhosis, with little or no fat infiltration, as well as the histologic differences between dietetic and cardiac cirrhosis, speak against the direct sequence of fat infiltration through anoxia to diffuse fibrosis of the liver It is more probable that fat infiltration and fibrosis of the liver are the juxtaposite results of more or less identical pathogenetic conditions, and therefore their simultaneous occurrence is more coincidental than obligatory The presence of widespread cellular necrosis in the liver of rats with dietetic cirrhosis[8] clearly indicates the presence of diffuse parenchymatous injury

Admittedly, the nonportal distribution of fibrosis in experimental cirrhosis in rats cannot be adjusted at the present time with the general claim regarding the portal origin of Laënnec's cirrhosis in man In far progressed cirrhosis the topographical origin of the fibrosis may not be determined with certainty The human necropsy material consists almost exclusively of such indecipherable pictures It is possible that a renewed study of human Laënnec cirrhosis in its early stages will confirm the conclusions drawn from animal experiments as to the nonportal origin of the fibrosis

TABLE 1

DIETARY FACTORS INVOLVED IN NECROSIS AND CIRRHOSIS OF THE LIVER

Effect on	Protein (Methionine Containing)	Methionine	Cystine	Choline	Vitamin E	Dietary Fat	Cod Liver Oil
Cirrhosis	Beneficial	Beneficial	Injurious	Beneficial	0	Injurious	Injurious
Necrosis (massive and zonal)	Beneficial	Beneficial	Beneficial	0 or injurious	Beneficial	0 or injurious	Injurious

The rather complicated interrelations between various dietary factors involved in the production or prevention of acute massive or zonal necrosis and cirrhosis of the liver are summarized in the following table

ENDOCRINE AND GENETIC FACTORS IN THE PATHOGENESIS OF HEPATIC INJURY

Dietary factors are mediated or influenced by endocrine and genetic factors in the development of, or in the resistance to, hepatic injury With regard to endocrine factors, it has been shown that under identical conditions female rats are more resistant to the production of toxic[31] and dietary[4, 32] hepatic injury, and at the same time respond more favorably to therapeutic dietary factors than male rats Furthermore, it has been demonstrated that goitrogenic substances, such as thiouracil[33] or propylthiouracil,[34] and estrogenic substances exert a beneficial, retarding effect on the production of dietary hepatic injury [32] Estrogenic hormones, especially ethinyl estradiol, seem to have also a lipotropic effect, which manifests itself especially clearly in the combined administration with methionine [35, 36]

The specific effect of goitrogenic substances on the liver may be related to their effect on thyroid function, specifically to the decreased metabolic rate including the metabolism of protein The high incidence of hepatic injury in clinical hyperthyroid conditions in man tallies well with the above animal experiments

The interrelation of estrogenic hormones and the liver found in animal experiments is in equally good accord with clinical observations The generally higher incidence of cirrhosis in males and the more recently observed malignant forms of chronic hepatitis, first observed during the last few years in Denmark[37] and Sweden,[38] in older women after the menopause are impressive illustrations for the protective role of the female gonads in hepatic injury

Genetic factors wield also an important, often decisive, influence on hepatic injury. Strains of the same species, for instance, rats of different breeds, may differ substantially in their resistance to the dietary factors instrumental in the production of necrosis,[5] cirrhosis,[32] or fat infiltration[39] of the liver In further consequence, it appears to be a logical postulate not to lose sight in the clinic of possible genetic variations, and not to expect perfectly uniform responses to a particular prophylactic or therapeutic regimen as applied to hepatic injury

TREATMENT OF EXPERIMENTAL HEPATIC INJURY

In general, dietary factors which assure prevention of a pathologic condition may not necessarily be beneficial in its treatment Regarding cirrhosis, prevention is synonymous with the maintenance of normal architecture and function of the liver In contrast, therapeutic factors have to exert their influence on a pathologically changed liver exhibiting various degrees of parenchymatous lesions (fat infiltration, necrosis, etc) and of fibrosis Furthermore, long standing experimental dietary cirrhosis is often associated in rats with secondary, but independent, pathologic changes involving parts of the endocrine apparatus, especially the gonads, and their secretion [39] In the presence of such pathologic changes, it is by no means certain that the utilization of dietary factors could proceed in the same manner as in preventive experiments on normal animals

In accordance with this presumption, the use of lipotropic factors (casein, methionine, choline), singly or in combination, in the treatment of dietary cirrhosis, has proved to be far from being uniformly effective In milder forms of dietary[32, 40] as well as of toxic experimental cirrhosis,[41] dietary lipotropic factors will bring about a reduction of the fat content of the diseased liver and restore hepatic cells to the normal state The reduction and even complete disappearance of histologically demonstrable fat infiltration may occur very soon after treatment is started This is in complete analogy to similar observations with the use of lipotropic factors in the therapy of human cirrhosis [42, 43] The initial improvement, however, is by no means always followed by regression of the basic, specific, fibrotic process It appears that lipotropic factors reduce fibrosis only when the latter is not too severe and widespread

Even in the case of mild, dietary cirrhosis in rats, successful therapeutic use of lipotropic factors requires three months or longer In *very severe* cirrhosis, as a rule, the effect of a lipotropic diet is disappointing Best therapeutic results may be obtained by the combination of an adequate amount of protein with methionine or choline or crude liver extract The treatment of very severe cirrhosis may require the interaction of further beneficial factors (nutritional and hormonal)

The fallacy of applying the results of preventive experiments to treatment is well illustrated by the role of thiouracil in the prevention and treatment of dietary hepatic injury In preventive experiments thiouracil has been found highly beneficial,[33] but in therapeutic experiments it was found to be, if anything, slightly injurious This observation may be interpreted as follows In the prevention of hepatic injury, lowering of the basal metabolic rate, under the influence of thiouracil, also lowers the requirement for lipotropic factors, but treatment of hepatic cirrhosis requires increased regeneration of hepatic parenchyma and high cellular activity for the regression of fibrosis—reactions for which lowering of thyroid activity should certainly not be conducive

The often observed superiority of protein *plus* methionine over protein alone in the treatment of experimental dietary cirrhosis may be due to the fact that in chronic protein starvation, which is the basis of dietary cirrhosis, protein, when given alone, will be used mainly for replenishing exhausted protein stocks or, in the growing organism, for growth, whereas methionine when given as a supplement to protein is available both for lipotropic activity as well as source of detoxifying sulfur-containing compounds (cystine) [44, 45] Conversely, lipotropic substances, such as choline or methionine, when given for the treatment of cirrhosis as supplement to a diet low in protein, will certainly not be able to improve the underlying condition of protein starvation With a great excess of protein it may be assumed that both requirements, i e , protein and source of lipotropic activity (methionine), will be covered However, in such an event a variable portion of surplus protein will be wasted

DIETETIC TREATMENT OF HEPATIC INJURY IN MAN

The pioneer observations of Patek clearly demonstrated that human hepatic cirrhosis is amenable to dietary treatment, and improvement of the clinical condition with apparent arrest of the pathologic process may thus be obtained [1, 2, 46] Patek used a nutritious diet rich in protein, supplemented with vitamin B concentrates, mainly with yeast [1]

Conclusions drawn from animal experiments seem to be in good accord with these empirical clinical findings In the treatment of hepatic injury a diet high in protein, with supplements of methionine (4 to 6 gm daily), choline (2 to 4 gm daily) and crude liver extract has proved its beneficial value both in man as well as in animals. It is not the purpose of this report to review all relevant clinical publications It suffices to mention only a few more recent papers[42, 43, 47] which are fairly representative for the great majority of similar clinical publications

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various manifestations in man have failed to make proper use of the model experiments in rats Provided that conclusions drawn from such experiments are applicable to human conditions, the treatment and prevention of hepatic injury in man may follow the following principles

1 Necrosis and cirrhosis do not respond to the same dietary factors In hepatic injury, which is, or might be associated with, zonal or massive necrosis, the interference of exogenous (virus such as in hepatitis, hepatotoxins such as carbon tetrachloride, chloroform, etc) or endogenous (in eclampsia, erythroblastosis) toxins should be suspected as the determining etiologic factors Even in diffuse fibrosis (Laënnec's cirrhosis), necrosis as a complication may supervene Once the liver cells are destroyed through the stages of degeneration and necrosis, therapy may only hasten regeneration of new hepatic parenchyma, but will not achieve direct repair of dead cells

Clinical management should therefore concentrate on the prevention of such serious complications as necrosis, or, if already present, on its containment This may be attempted by a diet high in sulfur-containing amino acids (methionine, cystine) and in tocopherol In practice, the procedure will consist of the administration of a diet high in protein (100 to 150 gm daily), supplemented by methionine (3 to 6 gm daily) and by tocopherol (100 to 300 mg daily) Our usual diet is rather low in tocopherol Choline *per se* will have no effect on necrosis Supplements of cystine, when given in moderate amount, should be beneficial in necrosis However, cystine when not simultaneously balanced by choline may aggravate fat infiltration and diffuse fibrosis (see Table 1), in addition to its nephrotoxic effect, and in consequence it is better avoided as a separate supplement

In the past, fat was generally looked upon as injurious in hepatic injury, especially in acute necrosis, as, for example, in acute hepatitis The diet, still commonly used in the management of infectious hepatitis and similar conditions, is characterized as high in protein and low in fat More recently Hoagland and his collaborators[48] have called attention to the fact that a diet low in fat is usually not very palatable, and will often be refused by patients with acute hepatitis, generally suffering from severe anorexia The same authors have also shown that a diet with unrestricted normal fat content is well tolerated by patients with infectious hepatitis, without any demonstrable untoward effect Here it may be added that in the diet Hoagland and his associates were prescribing, the fat was represented chiefly by milk fat According to the animal experiments there are distinct differences between the various fats regarding their possible effect on the liver Both necrosis and cirrhosis may be promoted by lard, and especially by cod liver oil, at least in comparison to vegetable fats and butter fat Thus, it appears that fats low in tocopherol, with a high content of unsaturated fatty acids, should better not be included in the diet of patients with acute or hepatic injury Such fats may even be more injurious after being heated during the preparation of food for human consumption Heated unsaturated

fats are apt to contain oxidized breakdown products which, in turn, may destroy tocopherol in the body [45]

In applying these considerations to clinical practice it is obvious that viral hepatitis, for example, once developed, will not greatly benefit by the administration of methionine, protein and tocopherol, and the duration of the disease will barely be shortened The only possible effect which may be expected from this treatment might be the increased resistance of still intact liver cells to the injurious effect of the spreading viral infection

It may be assumed that the fatal outcome of Rh-sensitization in the newborn infant is due mainly to severe injury of the liver (necrosis) Protection of the fetal liver may be attempted by administration of methionine and tocopherol to the pregnant mother Philpott and his associates[50] have reported recently on observations with methionine prophylaxis alone Their results appear to be promising and warrant further extension

2 In accordance with the corresponding animal experiments a diet high in protein and in lipotropic factors will materially reduce the fat content of a cirrhotic liver in man [42 43 47] This beneficial dietary effect, however, should not be construed as a sure sign of over-all progressive improvement In very severe cirrhosis, not only in animals but apparently also in man, the repair process may stop for a long, almost indefinite time at this stage, and thus the treatment may be considered as a failure On the other hand, in mild or moderate cirrhosis in man, diet forms which were found to be effective in the treatment of experimental cirrhosis may initiate, apart from the fat reduction, progressive regeneration of hepatic parenchyma, definite reduction of fibrosis, and—if the analogy with observations on animals applies—will lead to complete reestablishment of normal hepatic architecture

It appears that the combination of a diet high in protein with supplements of lipotropic substances (choline, methionine) will enhance protein retention in patients with hepatic injury, over and above the positive nitrogen balance achieved by a high protein, high vitamin intake alone [51] In animal experiments combination of protein and lipotropic substances has proved to be in general superior also to a protein diet alone, as measured directly by the improvement of the pathologic changes in the liver

Arrest or regression of cirrhotic changes when achieved requires a prolonged period of treatment The practical conclusion is obvious and unfortunately still often disregarded in clinical practice Even if we do not resort to the probably fallacious comparison of the life span of rats with that of man, the time required for the successful treatment of cirrhosis in man must be measured in months and years, not in weeks This must be especially true for cases in which the history may be traced back several years It is unfair to criticize the validity of conclusions reached in animal experiments for human conditions without having given them the proper clinical trial

As in severe cases of experimental cirrhosis, a diet high in protein and in lipotropic factors will often fail to secure improvement of severe human cirrhosis It is conceivable that far advanced cirrhosis requires some additional dietary factors or the interaction of endocrine factors in order to assure the desired therapeutic result It is hoped that in the future the combination of dietary and hormonal treatment will materially improve the outcome of therapeutic or prophylactic efforts in the management of hepatic injury in man

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SPRUE A CONSIDERATION OF ETIOLOGY, DIFFERENTIAL DIAGNOSIS AND MANAGEMENT

THOMAS M DURANT, M D , F.A C P * AND LOUISE A. ZIBOLD, M D †

INTRODUCTION

Although excellent reviews of sprue have appeared in the literature in recent years,[1–11] a concise presentation is felt to be important at this time for the following reasons

1 Sprue is a disease which is not limited to the tropics It may originate in the temperate zone, or it may be seen in missionaries and other who have returned from the tropics

2 Because of the supposed rarity in northern latitudes, the diagnosis of sprue is often not considered, and the disease is allowed to advance to a late stage with multiple deficiencies before therapy is instituted, such late treatment is often relatively ineffectual [7]

3 Sprue is often confused with other syndromes presenting diarrhea, glossitis, anemia, malnutrition, pigmentation or skeletal decalcification

4 Its close relationship to other macrocytic anemias provides interesting sidelights on the etiology of this group of anemias

DEFINITION

Sprue is a noninflammatory condition, often chronic and recurrent, characterized by glossitis, steatorrhea, macrocytic anemia and emaciation The pathophysiology consists in a profound disturbance of intestinal absorption believed by most authors to be secondary to a deficiency state The nature of the deficient factor remains obscure

Tropical sprue, nontropical sprue and celiac disease are identical disease entities modified by age and climate This group has been included under the term "primary sprue,"[12] there being no definite pathologic lesions which might account for the intestinal malfunction Secondary sprue has been the designation applied to the syndrome when it results from gross pathologic changes in the small bowel and the mesenteric lymphatic system [12]

ETIOLOGY AND PATHOGENESIS

It has been relatively easy to trace most of the manifestations of the full blown sprue syndrome directly to disturbed small bowel motility and absorption There is evidence that failure of phosphorylation, a

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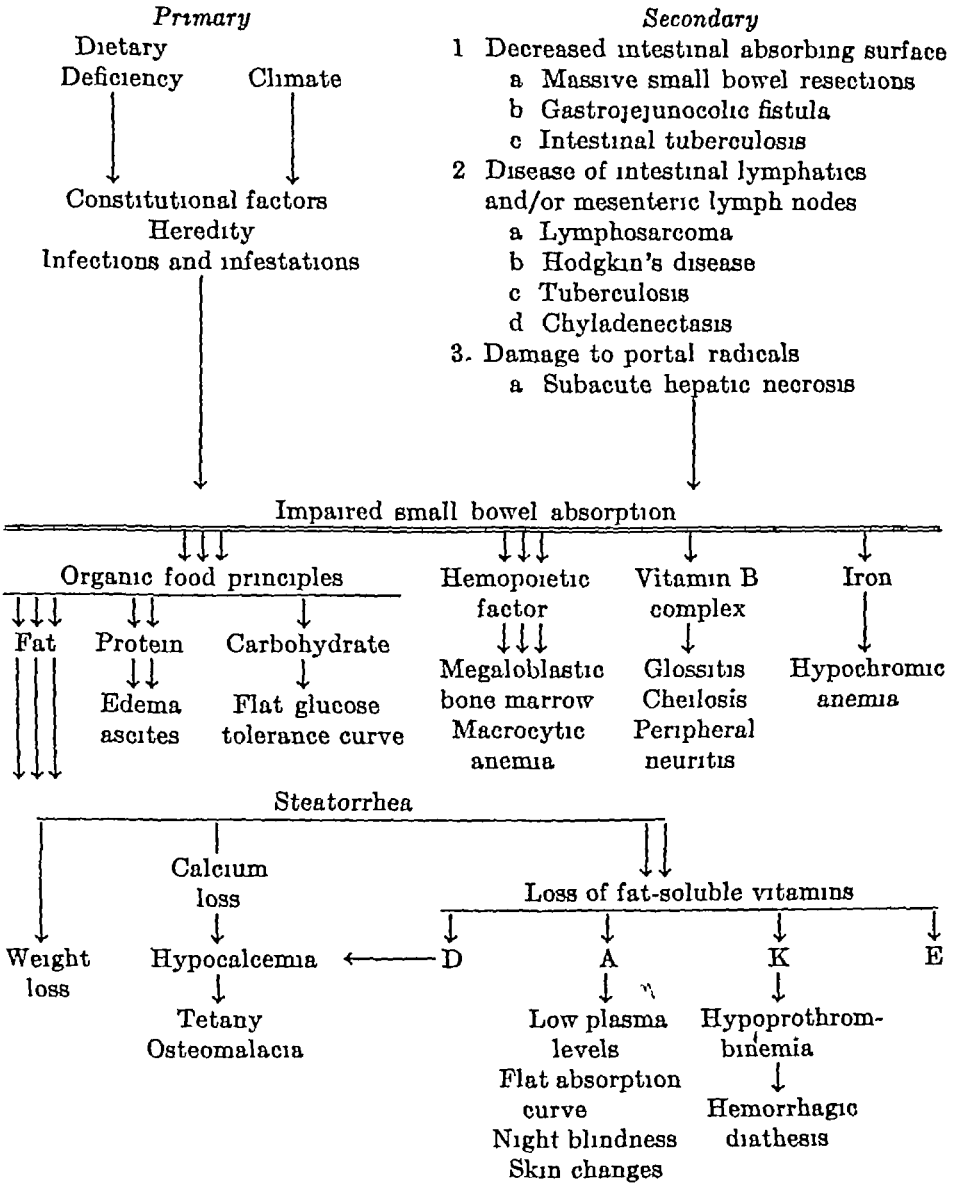
process necessary for the absorption of fatty acids, glycerol and glucose, is the underlying physiologic derangement,[13] but how or why this comes about is not clear Inadequate diet has been implicated repeatedly as an

TABLE 1

POSTULATED FACTORS IN THE ETIOLOGY AND PATHOGENESIS OF SPRUE



etiologic factor, particularly in the tropics where the consumption of good biologic protein is strikingly low It is of interest in this connection that the diet usually consumed by Cuban peasants, among whom sprue is common, was found to be almost completely lacking in folic acid by Angulo and Spies, who could produce remissions of the disease by giving

folic acid without changing the food intake[14] Dietary deficiency, however, is not the entire answer Most people on a deficient diet do not develop sprue, while in many instances the disease appears among those apparently well nourished Wartime experiences in India again reveal the close relationship of climate and season to incidence[10, 11] Explosive outbreaks of acute sprue among service personnel with an attack rate as high as 50 per cent in some units[15] revive interest in the old theory of infection Others[16] feel that sprue may be the result of a genetic defect of the bowel with diet, climate, season and infection playing secondary or modifying roles.

However the sprue syndrome is initiated, once it exists, it tends to perpetuate itself Impaired absorption causes anorexia, gastrointestinal discomfort and painful glossitis The patient, therefore, limits his food intake and thus increases already existing deficiencies which, in turn, intensify the symptoms of the disease The longer this vicious cycle persists, the more difficult it becomes to reverse the process The broad implications of the syndrome from the postulated primary etiologic factors to the full blown disease state are shown in Table 1

CASE REPORTS

Many of the classical features of sprue are illustrated by the following cases

CASE I —R. M., a 48 year old white man, had subsisted on a milk- and meat-free diet for eight years After five years of dietary restriction he developed what was thought to be primary pernicious anemia Liver extract was given irregularly Five months before admission to the hospital the patient was seized suddenly in the middle of the night with an explosive bout of diarrhea with the passage of pale, liquid, foamy, foul smelling stools The diarrhea persisted with 6 to 8 similar stools each twenty four hours, usually at night A red, sore tongue, which made hot liquids unbearable, soon appeared, and paresthesias of the hands became troublesome The patient rapidly lost weight and strength and upon hospitalization was cachectic. Pallor, gaseous abdominal distention and ankle edema were present Profound weakness, hypotension and darkened skin suggested Addison s disease There was no evidence of tetany Laboratory studies revealed a severe macrocytic anemia, hypochlorhydria, a flat glucose tolerance curve and markedly elevated fecal split fats on a controlled diet The serum calcium was 6.8 mg per 100 cc. and the phosphorus, 2 4 mg per 100 cc The total protein was 4 5 gm per 100 cc with a serum albumin of 3 gm The prothrombin was normal Roentgenographic studies of the small bowel revealed a "deficiency pattern" (coarsening or smoothing out of the valvulae conniventes, especially of the jejunum, with clumping of the barium in sausage-shaped masses in the lower jejunum and ileum secondary to spasm and dilatation) There was no x ray evidence of skeletal decalcification Therapy consisted of a high protein diet brewer s yeast and liver extract The patient had marked subjective relief, diarrhea ceased, glossitis cleared and weight gain progressed rapidly Hematologic improvement was far less rapid

CASE II —H D , a 51 year old white missionary, was well until the age of 32, when, while stationed in the Philippines, he developed abdominal pain and distention, postprandial nausea, diarrhea with six to seven foamy, fatty, foul

smelling stools a day, sore tongue and weight loss Liver extract and a low fat, low carbohydrate diet produced a remission Since the initial attack there have been numerous exacerbations, usually precipitated by an infection such as influenza or malaria Each time response to liver extract and diet was good Symptoms between attacks were minimal The patient was remarkably symptom-free for a three year period while a Japanese prisoner-of-war After release, however, as soon as a full diet was resumed, there was a very severe recurrence of the full-blown syndrome At the time of admission to the hospital, the patient was having five to six bulky stools a day and a moderate amount of abdominal discomfort The only abnormal laboratory finding was a high fecal fat content (6 1 per cent of the wet weight, 44 per cent of the dry weight) There was dramatic symptomatic relief after folic acid therapy, and the stools became normal

TABLE 2

PRIMARY PERNICIOUS ANEMIA, NUTRITIONAL MACROCYTIC ANEMIA AND SPRUE

Condition	Dietary History	Weight Loss	Glossitis	Diarrhea	Neurological Disturbances	Achlorhydria	Glucose Tolerance curve	Fecal Fat	Carotene & Vitamin A Levels	Fat & Vitamin A Tolerance Curves
Primary pernicious Anemia	–	–	+++	+ responds to HCl	Postero-lateral sclerosis	Always	Normal	Normal	Always	Normal
Nutritional macrocytic anemia	+++	+	+++	++	Peripheral neuritis frequent	Occasionally	Normal or high	Normal	Low	Normal
Sprue.	±	+++	+++	+++ Steatorrhea	Peripheral neuritis occasionally	Occasionally	Flat	Increased	Very low	Flat

DIFFERENTIAL DIAGNOSIS

When the sprue syndrome is in an advanced state with full-blown symptomatology, diagnosis is easy Often, however, symptoms related to a single deficiency so predominate the clinical picture that the underlying disorder is not suspected Therefore, the various manifestations of the disease will be considered separately in discussing the differential diagnosis

Macrocytic Anemia.—The three principal macrocytic anemias are primary pernicious anemia, sprue, and nutritional macrocytic anemia which includes the macrocytic anemias of pregnancy and pellagra They are hematologically indistinguishable The clinical similarities and differences[17, 18] are summarized in Table 2 Other causes of macrocytic anemia which at times may lead to confusion are extensive liver disease, carcinoma of the stomach and total gastrectomy

Steatorrhea.—Steatorrhea associated with pancreatic disease, usually chronic pancreatitis, produces stools which are grossly similar to those

of sprue However, the excess fecal lipid is neutral fat unsplit for lack of pancreatic lipase As in sprue, deficiencies secondary to loss of fat-soluble vitamins develop Differentiation (Table 3) is most important since therapy in the two conditions is fundamentally different

Skeletal Decalcification—In the tropics sprue is rarely complicated by symptoms of D avitaminosis, apparently because of abundant synthesis of the vitamin from sunlight In the temperate zone, however, the presenting features of a case may be tetany, bone pain, generalized skeletal demineralization, or spontaneous fractures frequently united by

TABLE 3

PANCREATIC STEATORRHEA AND SPRUE

Condition	Fecal Fat	Pancreatic Enzymes	Gastric Acidity	Glucose Tolerance	(X-ray) Pancreatic Calcification
Pancreatic steatorrhea	Neutral	Markedly decreased	Normal	Normal or diabetic	Frequent
Sprue	Split, soaps and fatty acids	Normal	Low	Flat	Absent

TABLE 4

DIFFERENTIAL DIAGNOSIS OF SKELETAL DECALCIFICATION

Cause of Decreased Bone Tissue	Calcium	Phosphorus	Alkaline Phosphatase
Osteoporosis deficient formation of bone matrix	Normal	Normal	Normal
Osteitis fibrosa generalisata increased bone resorption (hyperparathyroidism)	High	Low	High
Osteomalacia failure of calcification of newly formed bone matrix	Normal or low	Normal or low	High

uncalcified callus as seen in Milkman's syndrome In such patients other symptoms of sprue are often most difficult to elicit The stools may be formed and still have a fat content sufficiently high to carry off ingested vitamin D It becomes necessary, therefore, in establishing the diagnosis, to eliminate other causes of osteomalacia as well as to rule out those conditions often confused with it Albright et al[10] have presented this material in a most excellent and comprehensive fashion, and it is from this work that Tables 4 and 5 are drawn

Pigmentation[11, 20, 21] Hyperpigmentation is found in about one third of all patients with sprue It occurs most commonly as well defined

muddy brown spots or patches which are scattered over the face, the dorsum of the hands and feet and, less often, over the abdomen and buttocks The distribution may be symmetrical At other times the pigmentation is diffuse and so intense that Addison's disease is suggested It is most unusual to find pigmentation of the mucosae in sprue Pigmentary disturbances which have been confused with sprue are listed and compared in Table 6

TABLE 5

TYPES OF OSTEOMALACIA SEEN IN THE UNITED STATES

(Modified from Albright et al [19])

Classification of Osteomalacia	Serum					Urine				Vitamin A and K Tests
	Alkaline phosphatase	Ca	P	CO_2	Cl	Ca	NH_3	Tit Acidity	Sugar Acetone	
1 Vitamin D lack										
a "Simple" vitamin D lack	H*	N or L	L	N	N	L	N	N	–	N
b Resistance to vitamin D	H	N or L	L	N	N	L	N	N	–	N
c Steatorrhea	H	N or L	L	N	N	L	N	N	–	L
2 Renal acidosis										
a Tubular insufficiency without glomerular insufficiency	H	N or L	L	L	H	H	L	L	–	N
b Fanconi syndrome	H	N or L	L	L	N	H	H	H	+	N
3 Idiopathic hypercalcuria	H	N or L	L	N	N	H	N	N	–	N
4 Osteitis fibrosa generalisata after removal of parathyroid tumor	H	L	L	N	N	L	N	N	–	N

* H = high, N = normal, L = low

TREATMENT

General Measures.—Physical and mental rest is of major importance in the management of the sprue patient Exacerbations are commonly precipitated by fatigue and worry, and therapy must often be intensified during periods of stress Bed rest is essential during the active phase of the disease Every effort should be made to avoid acute infections which frequently bring on attacks Malaria is a particularly common offender in the tropics, and patients may prove refractory to treatment until antimalarial therapy is instituted [10]

Diet, Vitamins and Minerals.—The diet in sprue should be high in

animal protein, low in fat and moderate in carbohydrate. Protein up to 170 gm in twenty-four hours may be given, with rare red meat making up a large portion The amount of fat must be regulated by the patient's tolerance Initially, reduction to 25 gm a day may be necessary to con-

TABLE 6

DIFFERENTIAL DIAGNOSIS BASED ON PIGMENTATION OF THE SKIN

Condition	Pigment	Microscopic	Other Differentiating Features
Sprue	Melanin	Nonspecific	Mucous membranes not pigmented
Addison's disease	Melanin	Nonspecific	Macrocytic anemia Steatorrhea Pigmentation of the mucous membranes Water excretion test Response to desoxycorticosterone acetate
Hemochromatosis	Melanin Hemosiderin	Nonspecific	Hepatomegaly Diabetes often present Detection of hemosiderin in skin
Arsenical pigmentation	Melanin	Specific	History of arsenical intake Trunk and proximal extremities affected most Arsenic content of skin
Acanthosis nigricans	Melanin	Specific	Pigmentation of mucous membranes Symmetrical, pigmented verrucous patches Internal neoplasms often associated
Xeroderma pigmentosum	Melanin	Specific	Usually begins in childhood Tends to affect exposed surfaces Malignant changes common

trol steatorrhea Gradually the amount should be increased to 70 gm so that the fat-soluble vitamins will not be excluded 220 to 250 gm of carbohydrate a day is suggested The use of monosaccharides instead of starches, which tend to become coated with fat and ferment, often de-

creases flatulence and diarrhea Fruit juices, strawberries and bananas are particularly well utilized because fructose absorption is normal Frequent small feedings are advisable at first As improvement occurs, the patient often develops a ravenous appetite Rapid increases in diet, however, especially the fat and protein components, must be avoided since exacerbation of the diarrhea may result Mild, early cases will respond to dietary therapy alone

The fat-soluble vitamins, A, D, K and E, should always be added when the patient is on a low fat intake over an extended period of time or when there is evidence of deficiency of any member of the group They are best absorbed when given midway between meals With severe hypocalcemia and tetany, vitamin D in doses as high as 500,000 units a day may be necessary to control symptoms Dietary calcium should be supplemented with calcium gluconate by mouth when obvious deficiency exists

Of the B complex vitamins, assays reveal sprue patients to be particularly deficient in thiamine and riboflavin, while nicotinic acid is less affected [22] The entire group, however, should be added An interrelationship and antagonism is believed to exist between members of the complex, and, occasionally, when one member alone is given in large doses, an imbalance leading to clinical deficiency of another may result Such secondary deficiencies have been reported following the use of folic acid [23] Brewers' yeast, when tolerated, has proved to be a rather satisfactory source of the vitamin B complex in sprue With severe deficiency syndromes more potent preparations must be supplied

Although clinical scurvy is not seen, vitamin C levels tend to be low in sprue,[22] therefore, the diet is usually supplemented by additional ascorbic acid HCl and iron as ferrous sulfate may be useful in correcting any tendency of the anemia toward becoming hypochromic

Antianemic Substances.—Before the isolation of vitamin B_{12}, liver was probably the most important single therapeutic measure available in the treatment of sprue Vitamin B_{12}, a pure chemical compound isolated from liver and the most potent antianemic substance per unit volume known, shows promise of at least duplicating the spectacular response of most cases of sprue to adequate doses of parenteral liver extract [24] The hematologic response to these antianemic substances is similar in sprue to that seen in primary pernicious anemia, with a reticulocyte peak appearing about the seventh day Clinical improvement parallels that of the blood picture Within a week appetite returns, glossitis fades and diarrhea lessens To control gastrointestinal symptoms, the dose of liver must be somewhat larger than that required to produce a hematologic remission At least 300 units over a two or three week period is recommended In some cases liver extract must be continued at regular intervals to prevent exacerbations The gastrointestinal symptoms tend to recur before the blood count falls and may be used as a guide to the frequency of injections The dose of vitamin B_{12} varies with the patient but appears to lie between 10 and 100 micrograms daily by injection[24] during the active stage of the disease

Folic acid produces striking general clinical improvement in sprue [25, 26] The hematologic response, however, is somewhat less satisfactory than that obtained with liver extract. The blood count does not quite reach normal values and macrocytosis tends to persist in the peripheral blood [16, 18] Folic acid has been used with greatest success in cases of tropical sprue with long histories of poor nutrition A daily oral dose of 10 mg has been found to produce a maximum effect, and 2 5 to 5 0 mg seems to constitute an adequate maintenance dose [26]

Thymine or 5-methyl uracil, when given in massive amounts (15 gm a day), will produce clinical and hematologic remissions in sprue [27] The drug has no advantage over other antianemic preparations and is impractical to use because of the high dosage necessary

Blood Transfusions—Blood transfusions are of great value when severe anemia exists. Some patients may be refractory to treatment until whole blood is given [11]

Chemotherapy—Recent reports on sprue in India show sulfaguanidine to be highly effective in arresting the diarrhea [10, 11] An initial dose of 4 gm followed by 2 gm every three hours for one day, then 1 gm every three hours for three days, was the dosage schedule used [11]

Refractory Cases.—Advanced cases of sprue with multiple vitamin deficiencies, hypoproteinemia and severely deranged calcium metabolism generally respond poorly to treatment A large number of the cases seen in the temperate zone fall into this group Cases of secondary sprue also tend to be refractory unless the basic pathology can be corrected

SUMMARY

1 Sprue is not limited to the tropics Its supposed infrequency in northern climates may lead to delays in diagnosis with progression of the disease to an irreversible stage

2 The etiology and pathogenesis are discussed, and two cases are presented

3 The disease must be differentiated from (*a*) other macrocytic anemias, (*b*) pancreatogenous steatorrhea, (*c*) other causes of skeletal decalcification, and (*d*) conditions associated with pigmentation of the skin

4 Treatment consists of the following

(*a*) Physical and mental rest

(*b*) High protein low fat diet, with vitamins added according to existing deficiencies

(*c*) Antianemic substances (liver extract, vitamin B_{12} and folic acid)

(*d*) Other measures such as iron, hydrochloric acid, blood transfusions, and sulfaguanidine

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SOME REFLECTIONS ON SENILITY AND NUTRITION FROM THE CLINICAL STANDPOINT

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The Shift in Age Distribution of Our Population—With an ever lengthening life's expectancy in this country and with an ever increasing proportion of elderly people in our population, an increasing amount of attention is being focused on the processes of senescence and senility Two new journals, one of Gerontology and the other of Geriatrics, have recently started publication, the U S Public Health Service has established a division of Gerontology in the National Institute of Health, much research is going on in the hope that important old age problems may be answered thereby and many communities are concerning themselves with matters related to the better housing and care of their aged citizens

The shift in the distribution of both our white and black population from youth to middle and old age has taken place largely because of increasingly effective facilities for the prevention and cure of infections and infectious diseases in infants, middle aged people, and the elderly It must be only in minor degree that the shift in the age distribution of our population has been influenced by the use of insulin in diabetes, by the availability of more elaborate and better surgical technics in older people and probably by the application of better hygienic principles for people generally in this country All the while not too much has been learned which has enhanced our understanding of arteriosclerosis, arterial hypertension, osteoarthrosis and cancer, all progressive diseases characteristic of senescence At least very little has evolved from extensive research in these fields as well as in matters relating to the experience of aging which has served to change the age pattern of our population

Complexity of Disease in the Aged—With reference to the above so-called degenerative diseases including diabetes, it is unfortunately common practice to regard the elderly patient as being ill of only one of them, usually that one whose symptom picture presents itself most prominently As a matter of fact, he or she ordinarily presents good evidence pointing to the presence of more than one and often all of these diseases, to say nothing of an added acute illness. In addition to this superimposition and overlapping of disease entities in old people, one must remember that their diseases are born of many causes, that different etiological factors prevail, and that their disease picture will vary from patient to patient Senescence then, with all of its potential disease possibilities, whether degenerative or not, is more complicated and con-

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trasts sharply with childhood and adolescence in this respect In the latter age periods diseases are usually exogenous, more obvious, single, and of recent origin, the onset and course tend to be acute or subacute and there is little variation from patient to patient

Poor Cellular Nutrition a Factor.—Although the diseases of old age are complex when considered from any standpoint, all sooner or later exhibit the effects of poor cellular nutrition Parenchymal cells are especially sensitive to the status of their milieu They are dependent for nutrition upon the substance of an intercellular matrix and any change here may make for disordered function and structural change For the full maintenance of good cellular function and structural integrity, it would seem highly important that food intake must be adequate quantitatively and qualitatively in every way The products of digestion must be effectively and efficiently distributed by the cardiovascular, lymphatic and blood systems and they must be utilized when so distributed Besides all of this, injurious metabolic products must not accumulate and thereby impair cellular activity So it would seem that, in its broadest sense, nutrition should be maintained at an optimal level if one is interested in the prevention of the degenerative diseases of old age, to say nothing of the prolongation of life, or if one must act when these diseases have taken on their irreversible roles

Optimal Diets.—The optimal level of nutrition for any one individual and particularly one who is aging is, unfortunately, a matter of uncertainty Leonard A Maynard, director of the School of Nutrition, Cornell University, is responsible for the following "Our understanding of nutritional requirements during the last half of life is much less than for the period of growth because we know less about tissue changes which are taking place A child falls down, jumps up and goes blithely on its way An old man falls down and breaks his hip What difference in physiochemical structure of bone is invoked? We understand the role of nutrition in building bone during growth but little about its possible contribution in retarding changes" Maynard and his collaborator McCay found in the course of a ten year study of adult nutrition that, on comparing the performance of a group of rats growing at a normal rate with a group made to grow slowly by restricting the caloric intake, those on the restricted diet lived longer and preserved some of their youthful characteristics longer These conclusions were so generally contrary to prevalent conceptions of nutrition that these men began a long-term study of the relation of nutrition to the physiology and pathology of middle age and old age Completing the preliminary phase of their program in 1941, they began a second project planned to run from ten to twenty years, to clarify such concrete points as the following the effect of the amount of water consumed on the life span, the relationship of body fatness and exercise to longevity, the effect of common salt and calcium phosphate upon aging, the optimum adult consumption of vitamins, the relationship of exercise at different periods of life to the development of senility and the psychology in aging rats

While the laboratory has been slow in unfolding the riddle of old age and its diseases, clinical observation and study have done no better in this regard A long-time experience with aged people in the Philadelphia General Hospital has not revealed the sort of a diet and practices which will guarantee for long life and the prevention of degenerative diseases For the most part, however, the aged persons in our institution are not overweight, and certainly not obese, which is to be expected Obesity shortens longevity chiefly because it calls for a metabolic rate far in excess of that required by ideally weighted individuals of the same age and sex Some of the elderly population of our institution have always been thin according to reliable testimony and at the same time are reported to have been "good eaters" with no peculiar dietary habits Others have obviously reached their old age in spite of eating food predominantly of one variety, usually carbohydrates, all of which may seem out of line with what is regarded as being healthful Others have obviously lost weight prior to their hospital admissions because of a food intake of calorie inadequacy Under such circumstances it frequently is difficult to decide whether the patient's disease has been responsible for anorexia or whether somehow or other appetite is paced to the ever decreasing energy requirements of old age, this being in effect an example of adaptation A goodly portion of the aged who have gradually lost weight have evidently been influenced in their dietary habits by disturbances of the psyche related usually to degenerative changes in the cerebrovascular supply Very few of our patients seem to have lost weight because of a background of poverty

So it would seem that aged patients arrive at a time in their lives when they require admission to a general hospital with various dietary histories in their pasts, and judging by the criterion of weight loss may or may not be in a good state of nutrition With the return of appetite as the disease state tends to improve some of the elderly patients will regain lost weight during a hospital stay—sufficient evidence that for a time before admission the patient was subsisting on an inadequate diet On discharge from the hospital such as these seem to look better and seem to be younger

Vitamin Supplements—Outright evidence of vitamin deficiency is not a prominent feature in the aged as we have observed them here in the hospital Occasionally conjunctival xerosis and follicular keratoses are found Sometimes these old people may exhibit fissuring at the angles of the lips, a degree of lingual atrophy or magenta coloring Frank pellagrous lesions, nutritional edema, or polyneuritis are seldom noted in the old patients, but are usually seen in those who have also been alcoholics Even though frank evidences of vitamin deficiencies are rarely found, we have thought it well to bear in mind that the aged probably plod along at a suboptimal vitamin level We feel, therefore, that a supplementary intake of vitamins is probably needed by the aged because they may require more vitamin B_1 if they are on a high carbohydrate diet, or if they fail to absorb, inadequately utilize, or overdestroy and

eliminate vitamins These same possibilities apply equally well to proteins, fats, carbohydrates, calcium, phosphorous, and minerals generally

The Difficulty of Distinguishing between Normal and Abnormal.—Clinically it is somewhat perplexing to know whether or not certain features which present themselves in our aged person should be counted as normal or abnormal For example, when is one to look upon a delayed sugar tolerance curve which one may discover in an aged person as evidence of real diabetes or even count it as potential diabetes, and when should one act thereon therapeutically. Obviously diabetes while being a disease of metabolism carries with it consequences of a disordered state of nutrition In the absence of normal criteria in this regard, it has seemed better to treat patients exhibiting any quantitative deficiency in carbohydrate metabolism as diabetics Until definite normals are established for senility it seems likewise better to regard evidences of renal dysfunction as signs of renal disease, electrocardiographic deviations from the younger adult normals as evidence of real heart disease, and any degree of anemia as abnormal and calling for an appropriate degree of treatment

Hopeful Aspects of Dietotherapy in Vascular Sclerosis.—Our old patients, as do those of all doctors, give one an impression that arteriosclerosis is part of the aging process because almost all of them present in some degree the presence of some type of vascular sclerosis Some of our patients of a well advanced age have degenerative vascular changes in a minor degree and such changes are similar to those observed in younger patients without any signs of senescence

The histories of our arteriosclerotic patients strongly point to a congenital background for their disease but other considerations would seem to place such patients in a metabolic order of an acquired type This makes the arteriosclerotic picture a more hopeful one from the preventive standpoint Lesions of arteriosclerosis are irreversible in spite of claims made by those who practice sympathectomies or prescribe rice-fruit diets for hypertension

It may then finally develop that diet and a way of life will serve, if not to prevent these vascular changes, at least to slow up the rate of their development A way of correcting faulty lipid metabolism may some day be discovered or a means of counteracting unusual hormonal activity may be evolved, or some new unknown etiological factor may be unearthed In any event there will always be the matter of nutrition to consider in its broadest implications When surveys will have been made of the life and dietary habits of a large portion of the population over a long period of time, and when laboratory research will have mastered the problems of nutrition in the aged, then the limits of life's expectancy will be increased by many, many more years

THE CLINICAL ADMINISTRATION OF VITAMIN K

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RELATION OF VITAMIN K TO PROTHROMBIN

One of the achievements in nutritional research has been the isolation of an antihemorrhagic substance which is essential for the maintenance of an adequate prothrombin concentration in the blood This has been named vitamin K for *Koagulation* vitamin

Vitamin K is utilized by the liver in the manufacture of prothrombin A deficiency of vitamin K is less common than interference with its absorption from the intestine or its utilization by the liver The level of plasma prothrombin concentration depends upon the absorption of vitamin K from the intestine and the functional capacity of the liver to utilize this vitamin The manner in which vitamin K contributes to the manufacture of prothrombin is not decided It appears that it acts as an enzyme or catalyst upon a substrate within the liver [1]

Prothrombin is of crucial importance in the clotting of blood Clotting takes place in two stages as illustrated by the formula

Prothrombin + Ca + Thromboplastin → Thrombin
Thrombin + Fibrinogen → Fibrin

The Prothrombin Time —Prothrombin cannot be measured quantitatively by any chemical test Its level in the blood is determined indirectly by the capacity of the blood specimen to initiate clotting when other factors are controlled

Prothrombin concentration bears no direct linear relationship to clotting time as measured by the usual method The clotting time of the blood may remain normal until more than 80 per cent of the prothrombin concentration is lost [2] Figure 271 illustrates this point

Only an indirect measurement of the prothrombin concentration is sensitive enough to anticipate the bleeding tendency when cruder measurements of the clotting time are normal Several methods are available for this measurement

Plasma Prothrombin Time of Quick.[3] This test is of great practical value and is sensitive enough to detect a prothrombin deficiency which is clinically important It has the advantage of simplicity

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It is a one stage method in which the amount of calcium and thromboplastin are kept constant by addition to the blood specimen The rate of clotting depends upon the concentration of prothrombin which is present The clotting time of normal plasma under these conditions varies, according to the activity of the thromboplastin used, between 10 and 25 seconds By using a control this wide factor can be translated into percentages of normal Between 70 and 100 per cent is a safe range of prothrombin concentration

The Two Stage Method of Warner, Brinkhous and Smith [4] This is a complex, time-consuming determination and offers no practical advantages over the one stage method It may detect moderate degrees of hypoprothrombinemia in cases of liver disease when the one stage method is inconclusive [5]

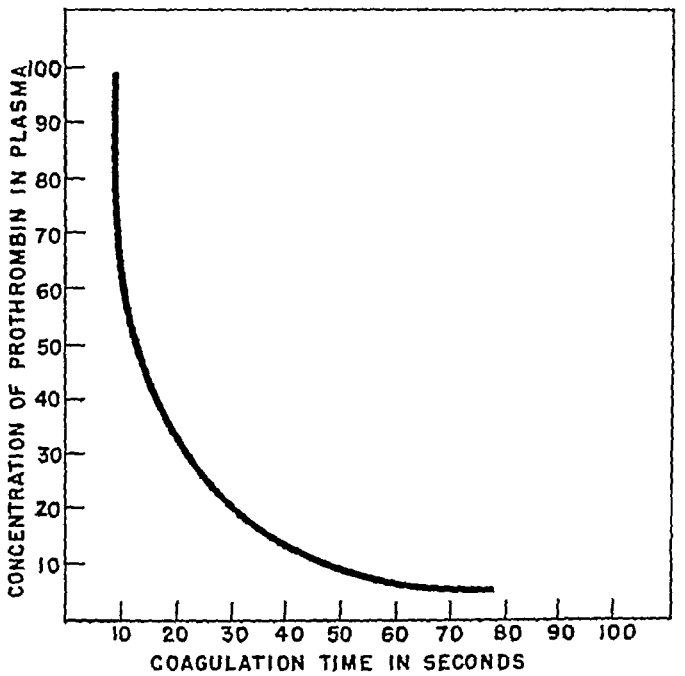

Fig 271 —No linear relationship between prothrombin concentration and clotting time is evident

The prothrombin in the blood specimen is first converted to thrombin with an optional amount of calcium and an excess of thromboplastin In the second stage of the test the amount of thrombin formed is measured by determining the highest dilution of the specimen which will produce clotting of a standard fibrinogen solution in a set period of time Prothrombin is measured in units, one unit being the amount required to form one unit of thrombin Human plasma normally contains 300 units per cc [6]

The "Bedside" Test This is the simplest and fastest method of determining prothrombin activity It eliminates the necessity for recalcification but it is a cruder measurement and does not directly represent the amount of prothrombin present in the blood A fixed amount of commercial thromboplastin is mixed with a drop of blood and the clotting time is measured The results are compared with the clotting time of a normal patient and are expressed in percentage of normal [7]

$$\text{Clotting activity (\%)} = \frac{\text{Clotting time of normal} \times 100}{\text{Clotting time of patient}}$$

The prothrombin concentration or activity is very constant in normal individuals It is not altered in the bleeding tendency associated with purpura or hemophilia There is a wide margin of safety in the prothrombin concentration Bleeding does not usually occur unless the concentration is below 20 per cent of normal The tendency to bleed at levels approximating this is accelerated by trauma or local tissue changes

The Nature of Prothrombin.—Prothrombin is in molecular association with blood protein but its exact composition is unknown It is formed within the liver and delivered into the blood where constantly lower levels are found as the blood circulates through the lungs [8] Evidence would suggest that there are no important stores or reserves of this substance

It is experimentally possible to lower the prothrombin concentration or increase the prothrombin time in several ways (1) by decreasing the intake of vitamin K, (2) by interfering with the absorption of vitamin K, (3) by administering spoiled sweet clover (dicoumarin), and (4) by injuring the liver directly [9]

Metabolism of Vitamin K.—The existence of vitamin K was first suspected by Dam In a study of lipoid metabolism, newly hatched chicks were placed on a fat-free diet After several weeks hemorrhages developed This observation prompted further study and led to the demonstration that an important fat-soluble vitamin was essential for the prevention of bleeding [10]

Vitamin K is a fat-soluble accessory food substance Bile is essential for its absorption from the intestine An important factor in its absorption is a physiologically and anatomically adequate intestinal tract Bacterial synthesis of this vitamin by organisms normally present in the intestinal tract is a major source of supply The condition of the liver and its ability to utilize the vitamin often determines the bleeding tendency in the absence of a vitamin K deficiency

The amounts of vitamin K required in the diet are small and probably are less than 1 mg a day Normal individuals on a vitamin K-free diet do not usually show any evidences of hypoprothrombinemia because intestinal organisms are active in the endogenous synthesis of the vitamin This source of the vitamin can be suppressed by intestinal sterilization There is marked depletion of prothrombin concentration following liver injury [11] Vitamin K concentrates added to prothrombin-deficient plasma do not improve the clotting time in vitro [11] The liver is apparently essential to the intermediary effect of vitamin K upon prothrombin concentration

Following the oral administration of vitamin K the effect upon the prothrombin concentration is usually manifested in twenty four hours if conditions favorable to absorption are present The effect following parenteral administration occurs in three to six hours

There are no toxic effects from the usual dosages of vitamin K The

large doses used in Dicumarol hypoprothrombinemia approximate the toxic doses used in experimental animals but have no actual toxicity in humans

Hyperprothrombinemia has been induced in human subjects by the administration of a vitamin K substance The small degrees of hyperprothrombinemia were measurable only with 12 5 per cent dilute plasma This change toward increased clotting met with resistance of increasing magnitude as it progressed The hyperprothrombinemia induced by vitamin K substance was ephemeral, while that present in certain clinical conditions such as peripheral thrombo-embolism continued for extended periods [18] With the use of undiluted plasma it is practically impossible to raise the prothrombin concentration above 100 per cent The observations that this could be done and measured by a more sensitive dilution has little importance when therapeutic doses of vitamin K are used

Pathology of Vitamin K Deficiency.—Experimentally produced hypoprothrombinemia from vitamin K deficiency results in hemorrhage, most marked in mucous membranes, skin, subcutaneous tissues, muscle, lungs, heart, spleen, brain and meninges Blood vessels are congested and dilated Their walls show changes ranging from swelling and degeneration to complete rupture Degenerative and reparative changes occur in tissues secondary to these initial changes Erosions are present and proliferation of capillaries may be seen Trauma plays an accelerating role in the bleeding that results from these pathological alterations [14]

Clinical Recognition of Vitamin K Deficiency.—The clinical manifestation of vitamin K deficiency is hemorrhage, and the most common site of hemorrhage is into areas of local trauma such as may result from accidental injury or operation Epistaxis, hematemesis, melena, hematuria and metrorrhagia are not unusual,[15] but hemoptysis is not common Bleeding into the urinary tract is more likely to occur if local changes are present Intracranial hemorrhages occur, as in the bleeding of the newborn

Bleeding into the skin is often the first sign to appear This commonly precedes other bleeding and may develop with unusual rapidity. Ecchymoses may develop which spread and become confluent They develop first over areas where trauma or pressure is applied Petechial hemorrhage is not so common

A severe hypoprothrombinemia without hemorrhage may be present until trauma occurs Wound bleeding after operation develops when no other manifestations are present The chances of gastrointestinal bleeding after operation are enhanced by the presence of a local lesion such as gastritis, varix, ulcer, or ulcerative colitis

Bleeding develops uncommonly from hypoprothrombinemia when the prothrombin concentration is more than 20 per cent of normal but rapid changes are possible A sudden drop to a critical level, where bleeding occurs, may develop in a few hours after what appears to be a satisfactory level

In patients with obstructive jaundice and hypoprothrombinemia, bleeding usually does not occur until after operation The prothrombin concentration reaches its lowest level one to four days postoperatively Bleeding may start as an oozing from the wound and there may be bleeding from mucous membranes or into the skin The danger of bleeding in these cases is not over until the tenth postoperative day [16]

Degrees of hypoprothrombinemia do not always parallel impairment of other liver functions In any case with suspected liver injury, before operation, a prothrombin determination must be made in the face of normal functions as measured by other tests

Natural Sources of Vitamin K.—Variable amounts of vitamin K are present in the following [17] alfalfa, kale, spinach, carrot tops, oat sprouts, soybean oil, tomatoes, cabbage, cauliflower, cereal grasses (oats and wheat) and hog liver

Vitamin K can also be prepared from fish meal and rice bran casein after these materials have been allowed to putrefy Bacteria effect this synthesis The vitamin is present in the lipoid fraction of many bacteria

Chemistry of Vitamin K and the Development of Substances with K Activity —Natural vitamin K appears to consist of at least two fractions Vitamin K_1 is present in the diet Vitamin K_2 can be produced by the putrefaction of fish meal and by bacterial synthesis in the human intestine The two fractions are closely related in chemical structure Each has an identical quinone nucleus and similar carbon units Vitamin K_1 has been produced synthetically and its formula identified as 2-methyl-3 phytyl-1,4-naphthoquinone

Following the announcement of the key position of the quinone molecule in this formula, an effort was made to test known substances having a comparable structure with reference to their antihemorrhagic activity [18]

This quest led to the discovery of two substances with vitamin K activity 2 methyl-3 hydroxy-1,4-naphthoquinone, and 2-methyl-1,4-naphthoquinone.

It was shown that 2-methyl-1,4 naphthoquinone, or menadione, had a greater antihemorrhagic potency than natural vitamin K, or any other substance with vitamin K activity [19] Menadione is a naphthoquinone derivative having the antihemorrhagic properties of vitamin K In no sense is it synthetic vitamin K It has become the prototype for the development of other substances with K activity

The utility of menadione has been further increased by the development of compounds of similar composition which are water soluble [20] These can be administered intravenously and can be given orally without the simultaneous administration of bile salts

Conditions in Which the Administration of Vitamin K Is Indicated — As there is no indication as to when K administration is needed except a prolongation of the prothrombin time, with or without bleeding, this determination must be done in all cases where the possibility of hypoprothrombinemia exists. The dangers of a low prothrombin concentration must be anticipated before clinical signs of deficiency appear

Among conditions in which hypoprothrombinemia may measure some defect in the metabolism of vitamin K are simple (idiopathic) K avitaminosis, hypoprothrombinemia of the newborn, hypoprothrombinemia of intestinal disorders, hypoprothrombinemia of biliary obstruction or fistula, hypoprothrombinemia of liver disease or injury, and hypoprothrombinemia induced by therapy

SIMPLE (IDIOPATHIC) K AVITAMINOSIS

An exogenous deficiency of vitamin K serious enough to lead to hypoprothrombinemia and bleeding is rare The adult requirement for vitamin K is so low that even the poorest dietary may contain sufficient amounts to prevent this In the presence of starvation, bacterial synthesis in the intestine supplies adequate vitamin K As in other deficiency states, no manifestations may be present until conditioning factors are added The onset of a severe diarrhea as part of the nutritional disturbance may precipitate the signs of a florid deficiency The oral use of drugs like streptomycin or sulfonamides may do the same thing in a patient with lowered prothrombin concentration but with nothing to suggest a deficiency The association of hepatic impairment may further condition a latent K avitaminosis

The Philadelphia General Hospital takes care of many indigent patients, and cases of malnutrition are always present on the wards It was possible to produce only one case of what appeared to be simple (idiopathic) K avitaminosis with bleeding in a two year search of hospital admissions

Case I —A P , a 60 year old white female, was admitted to Philadelphia General Hospital on March 31, 1948 The history, obtained from the family, revealed that since 1925 the patient had periods of depression in which she refused to eat The last of these periods began three weeks prior to admission and since then she had eaten nothing She became weak and appeared to lose weight rapidly Physical examination on admission showed the patient to be very emaciated The temperature was 97 4, pulse 88, and respirations 25 The blood pressure was 100/55 There were several petechiae on the bulbar and palpebral conjunctivae There were numerous petechiae and ecchymoses on the gingiva, the tonsillar fossa and palate There was bright red blood in the oropharynx and the tongue was dry, smooth and beefy red The heart and lungs were normal The skin of the lower abdomen and extremities showed a uniform distribution of petechiae and ecchymoses There was slight pitting edema in the pretibial areas There were large ecchymotic areas on both labia majora and numerous petechiae on the vaginal wall, with oozing of bright red blood Rectal examination revealed black feces and blood on the examining finger

The urinalysis was negative The serum albumin was 3 2 gm and the serum globulin 1 6 gm per 100 cc The hemoglobin was 6 5 gm and the red blood count was 2,070,000 The reticulocytes were 7 5 per cent and the platelets were 214,000 The serum bilirubin was 0 3 mg per 100 cc , the flocculations were negative, and the bromsulfalein test showed 8 per cent retention after forty-five minutes

The bleeding and coagulation times were normal The prothrombin concentration on April 1 was 20 per cent of normal

At this time sigmoidoscopic examination revealed mucosal bleeding and induced bleeding from the slightest application

The patient was given multiple vitamin capsules, ascorbic acid, 100 mg , and ferrous sulfate 0.32 gm three times a day Tube feedings of a high protein, high vitamin formula were started She was given 5 mg of Synkayvite intramuscularly twice a day On April 5 the prothrombin determination was 51 per cent of normal The petechial and ecchymotic areas had faded There was no longer active bleeding in any area. Two units of citrated whole blood were given, the first on April 6 She improved in strength, ate better and became ambulant She appeared more alert and showed an interest in her surroundings After five days 5 mg of Synkayvite was given once daily

On May 2 the prothrombin time was 100 per cent of normal. The hemoglobin was 10.2 gm , the red blood count was 4,010 000, the serum albumin was 3 9 gm and the serum globulin 2 4 gm. per 100 cc

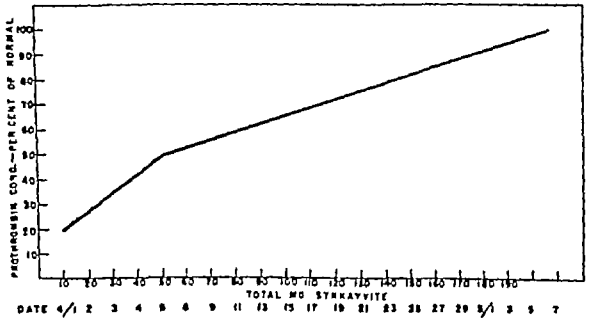

Fig 272 (Case I) —Simple K avitaminosis, showing response of hypoprothrombinemia to Synkayvite

At the time of these determinations there were no residua of the previous bleeding and active bleeding did not occur The patient was transferred to the neuropsychiatric division before other studies were done

Comment —This patient, in what appears to be the absence of conditioning factors, developed hypoprothrombinemia and hemorrhage from starvation She showed a rapid response to general nutritional care and the specific use of a substance with vitamin K action There was no gross evidence of hepatic impairment The sites of hemorrhage were those frequently seen in hypoprothrombinemic bleeding, the skin and the mucous membranes We cite this as an unusual case in that the prothrombin levels fell so low and bleeding occurred from simple starvation Other cases of nutritional deficiency may have prothrombin levels between normal and this critical point and will suffer the risk of hemorrhage only after a precipitating factor has been added

HYPOPROTHROMBINEMIA OF THE NEWBORN

During the first days of life the prothrombin concentration may fall precipitously This decline usually reaches its lowest level in three or four days and after this the concentration rises slowly. After the first week the infant is almost always out of danger of bleeding [21] Most infants go through this period without any hemorrhagic manifestations, but with trauma or rough handling bleeding may result The number of cases with actual bleeding from hypoprothrombinemia is about 1 per cent of all newborn Hemorrhages may occur in the cranium, the skin, the retina, mucous membrane, or the umbilical segment

The hypoprothrombinemia of the newborn is due to several factors The most important of these are decreased storage of vitamin K in the fetus and the absence of an intestinal bacterial colony in the first days of life

Not all hemorrhagic manifestations in the newborn are due to hypoprothrombinemia However, the frequency with which the prothrombin concentration drops in the neonatal period makes it likely that some infants are in danger of bleeding from this cause This low prothrombin concentration can be corrected by the administration of vitamin K to the mother in the immediate prenatal period or to the infant in the first few days of life [22]

Case II —B Y , a colored infant, was born of a 25 year old mother who had received no vitamin K preparation ante partum The infant was born full term by a spontaneous right occiput anterior delivery Labor lasted twenty hours and fifty minutes The birth weight was 6 pounds, 8 ounces The condition at birth was good, breathing was not delayed and there were no gross abnormalities Following delivery, there was a postpartum hemorrhage from the mother of about 400 cc

Two days after delivery it was noted that the infant's feces contained bright red blood The hemoglobin was 6 5 gm , the red blood count 1,830,000, the white blood count 19,000 and the differential count was normal The prothrombin concentration was 14 per cent of normal

The infant was given Synkayvite, 2 mg intramuscularly, and 30 cc of citrated whole blood The following day the stools were free of gross blood The dosage of Synkayvite was repeated for five days Following this the prothrombin concentration was 100 per cent of normal There were no further hemorrhagic manifestations and mother and child left the hospital in good health

Comment. This case illustrates the need for prophylactic control in the last few days of pregnancy The prompt response to the parenteral administration of a vitamin K substance is characteristic of hypoprothrombinemia of the newborn After the first critical days the infant is capable of handling its own requirements for vitamin K The need for correction of a deficiency is over once the prothrombin concentration has returned to normal

HYPOPROTHROMBINEMIA OF INTESTINAL DISORDERS

A vitamin K deficiency with hypoprothrombinemia develops from this cause when there is an alteration in the absorptive surface of the

bowel or where hypermotility interferes with absorption of the vitamin These mechanisms may result from intestinal disease, resection, fistulization or prolonged diarrhea

Sprue, regional enteritis and enterocolitis, ulcerative colitis and the

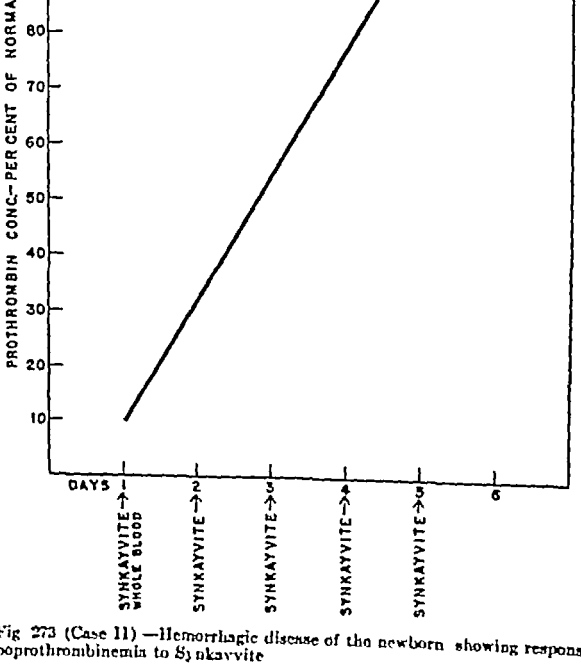

Fig 273 (Case 11) —Hemorrhagic disease of the newborn showing response of hypoprothrombinemia to Synkavvite

dysenteries may all result in hypoprothrombinemia Resection of large areas of the small intestine with entero-enterostomy or enterocolostomy may lead to a deficient absorption of vitamin K and a bleeding tendency The steatorrhea of pancreatic insufficiency may lead to the same result but this is a much less frequent cause The diarrheas of moderate dura

tion do not interfere with the absorption of vitamin K in a degree to cause hypoprothrombinemia

Bleeding due to intestinal ulceration may be intensified by an associated hypoprothrombinemia In chronic intestinal disease or derangement there may be hepatic dysfunction which in itself will interfere with the metabolism of vitamin K. As many of these patients receive drugs which suppress intestinal bacteria, there is added this other potential cause of hypoprothrombinemia It is necessary to follow these cases with repeated determinations of the prothrombin concentration This is particularly so when operation is contemplated A mild hypoprothrombinemia may be present which may drop rapidly after operation to a level at which bleeding occurs

CASE III L C , a 36 year old female, was admitted to the Abington Memorial Hospital on February 19, 1949, in premature labor She delivered an infant after seven months of pregnancy shortly after admission There was no bleeding in the infant

In August 1948 the patient noted the onset of cramping, lower abdominal pains and nausea with vomiting Shortly after this swelling of the hands developed The bowels were very loose and watery and their odor was foul No blood, mucus, or pus were seen There was a moderate elevation of temperature Headache was present

The symptoms were considered to be the result of a toxemia of pregnancy However, no hypertension was present and the results of urine examination were not recorded

For the next few months the patient had remissions and exacerbations of her diarrhea At times the discharges were very frequent and attended with lower abdominal pain The diarrhea resisted all measures of therapy

After the delivery of a premature infant, the patient was transferred to the medical service The temperature at this time was 103, the pulse 100, respirations 2 8, and blood pressure 125/75 The abdomen was moderately distended and peristalsis was active There was marked tenderness, especially in the lower part, but no rebound tenderness The uterus was four fingers above the symphysis There was exquisite perirectal tenderness and a tender mass was felt in the cul-de-sac The day after this examination there was a great deal of purulent discharge from the rectum and vagina A fistula developed between the anterior rectal wall and the vagina Following the spontaneous drainage of this abscess the patient showed marked improvement and the temperature became normal The diarrhea lessened and finally stopped

Urinalysis showed a moderate amount of albumin and many white blood cells The hemoglobin was 10 gm , the red blood count 3,180,000, the white blood count 13,950 with a normal differential count, and the blood urea nitrogen was 26 mg per 100 cc The serum bilirubin was 1 5 mg per 100 cc and the flocculations were negative The serum albumin was 3 04 gm and the serum globulin was 1 98 gm per 100 cc Stool, urine and vaginal cultures showed B coli Stools were 4 plus for occult blood No ova and parasites were found A bromsulfalein test showed 20 per cent retention in forty-five minutes The prothrombin concentration was 53 per cent of normal The next day (February 22) the prothrombin concentration was 23 per cent of normal The patient was given streptomycin 0 5 gm intramuscularly twice a day and penicillin 200,000 units twice a day Synkayvite, 20 mg subcutaneously daily, was started on February 25 On February 28 the prothrombin concentration was 79 per cent of normal.

At the time of this report the patient is much improved, having only occasional cramping and looseness of movement. Studies of the small bowel and colon were to be undertaken as recovery continued

Comment—The severe diarrhea lasting for a long period in this case interfered with the absorption of vitamin K If disease of the wall of bowel is also present, then this additional factor would interfere with its absorption No peroral sulfonamide or streptomycin were given The administration of parenteral streptomycin would not depress intestinal synthesis of the vitamin The evidence of hepatic dysfunction as suggested by the positive bromsulphalein test could in addition retard the synthesis of prothrombin in the liver Recovery followed the drainage of a purulent collection and the cessation of diarrhea The improvement in prothrombin concentration was further stimulated by the parenteral administration of a substance with vitamin K action

HYPOPROTHROMBINEMIA OF BILIARY OBSTRUCTION OR FISTULA

In patients with biliary obstruction or fistula an absence of bile salts in the intestine leads to a defect in the absorption of vitamin K and hypoprothrombinemia In biliary tract disease with jaundice, even in the absence of complete obstruction, a diminished bile salt concentration in the bile may lead to the same result In these cases the chances of hypoprothrombinemia and bleeding is further enhanced by a diminished food intake, vomiting, secondary liver injury and the use of drugs which may depress intestinal bacterial synthesis of vitamin K There is no evidence that a deficit of calcium or fibrinogen contribute to the bleeding of the patient with biliary tract disease and jaundice

A great deal of importance must be attached to the presence of secondary liver injury in cases of prolonged and intermittent obstruction These cases may not show an adequate response to the administration of vitamin K Correction of hypoprothrombinemia will require the addition of therapy directed at the restoration of liver function, the use of blood as a direct supply of prothrombin, and the relief of the obstruction

Bleeding is most likely to occur in the first four days of the postoperative period 1 or at least ten days after operation the prothrombin time must be measured at repeated intervals Spontaneous bleeding in these patients may occur before operation and without any trauma However, the effects of blood loss, plasma dilution and depression of liver function by handling, anoxemia or anesthesia, accelerate the tendency to bleed in the postoperative period The postoperative fall in prothrombin concentration after operation is transitory in most cases, and where the levels do not reach less than 20 or 30 per cent of normal, bleeding may not occur[22] The majority of patients with jaundice do not bleed postoperatively because this margin of safety has not been crossed

The tendency to bleed after operation may be suspected by a moderate reduction in the prothrombin concentration What appears to be a safe concentration may fall rapidly within a few hours, and serious bleeding will occur The prothrombin concentration is a labile and sensitive index

in these patients The danger of bleeding from an associated esophageal or gastric varix, ulcer or neoplasm is greatly increased by the hypoprothrombinemia of biliary obstruction or fistula

There is often no direct correlation between the degree of jaundice and the prothrombin concentration However, low levels are usually found in patients with more severe degrees of jaundice

Spontaneous bleeding may occur into the skin, muscles and gastrointestinal tract Epistaxis is common in this type of hypoprothrombinemic bleeding An oozing of blood from the wound or bleeding into the peritoneal cavity are common postoperative sites In many patients with jaundice the stools are consistently positive for occult blood In some of these the blood will disappear after the administration of vitamin K In the absence of any local cause it is likely that the passage of food residues acts as a traumatic factor in a patient whose prothrombin concentration has been lowered

The exclusion of bile from the intestine by an external biliary fistula in an experimental animal will lead to impairment of vitamin K absorption and a rapid fall in the prothrombin concentration This may be corrected by the re-feeding of bile Correction of the fistula and treatment of any secondary liver injury will speed recovery External biliary fistulas with complete exclusion of bile from the intestine are not common in humans Such a case would require careful attention to the prothrombin concentration

Case IV —A C , a 55 year old male and a known diabetic, was admitted to the Philadelphia General Hospital on April 30, 1947, following an attack of colicky abdominal pain Shortly before admission his skin became deeply yellow and his stools were clay-colored Physical examination on admission was negative except for marked jaundice and clay-colored feces on the gloved finger examination of the rectum A few days after admission the liver edge was felt one finger below the ribs It was smooth and nontender

The urinalysis showed a 2 plus test for reducing substances and was positive for bile and urobilinogen Acetone and diacetic acid were not present The serum bilirubin was 14 mg per 100 cc The serum albumin was 3 8 gm and the serum globulin was 3 6 gm per 100 cc The thymol turbidity was 4 7 units and the thymol flocculation was negative The cephalin-cholesterol flocculation was 3 plus in forty-eight hours The serum cholesterol was 373 mg per 100 cc and urine urobilinogen was 2 7 Ehrlich units The prothrombin concentration was 25 per cent of normal

The patient was given 20 mg of Synkayvite intramuscularly at once and 5 mg intramuscularly each following day until May 24

Following this and measures to improve hepatic function the serum bilirubin was 24 5 mg per 100 cc , urine urobilinogen 6 0 Ehrlich units, and the prothrombin concentration rose to 100 per cent of normal On the day before operation the concentration had dropped to 64 per cent of normal

The patient received no Synkayvite from May 24 until May 27, the day a cholecystostomy was performed Granular concretions and large pigmented stones were removed The liver was hard, finely granular, yellow-green in color, with large dark punctate areas on its surface The wound area was dry at operation, no areas of bleeding were noted and the patient was returned to the ward in good condition

About five hours after operation considerable bloody drainage was noted from the wound area He was given 500 cc of citrated whole blood and 10 mg of Synkayvite The dressings were reinforced but bleeding continued, and nine hours later the patient went into shock He was given 500 cc of citrated whole blood and Synkayvite 10 mg intravenously and intramuscularly A second unit of blood was given but was discontinued after 250 cc. had been used because of a reaction He was given 500 mg of ascorbic acid subcutaneously and 10 mg of Synkayvite intramuscularly every two hours After three doses of Synkayvite the bleeding stopped and another 500 cc. of citrated whole blood with two units of plasma were given without reaction. A prothrombin concentration four hours after the last dose of Synkayvite was 84 per cent of normal

The patient continued to receive daily parenteral Synkayvite therapy and there were no further evidences of bleeding In spite of this the prothrombin con

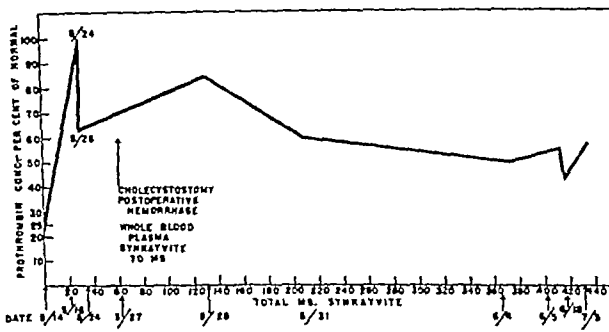

Fig 274 (Case IV) —Showing tardy and inadequate response of the prothrombin concentration to vitamin K therapy after cholecystostomy with postoperative bleeding

centrations remained lowered During this same period the serum albumin was 1 9 gm per 100 cc. and the cholesterol esters were 45 per cent of normal All flocculation tests were negative On July 5 the prothrombin concentration was 60 per cent of normal and on that day a midthigh amputation for gangrene was performed There was no excessive postoperative bleeding

Comment —This case had intrinsic liver damage as suggested by the low serum albumin, the increased excretion of urobilinogen in the urine and the low cholesterol esters A false sense of security was given by the immediate response of the prothrombin concentration to vitamin K therapy Not only should therapy have been continued in the immediate preoperative and postoperative period but the high preoperative urobilinogen content in the urine should have directed more attention to impairment of liver function The tardy and inadequate response of the prothrombin concentration after operation further illustrates the effect of depressed liver function on prothrombin concentration

HYPOPROTHROMBINEMIA OF LIVER DISEASE OR INJURY

The plasma prothrombin concentration may be decreased experimentally by hepatotoxins such as chloroform, carbon tetrachloride and phosphorus, and there will be no response to vitamin K therapy [9] Hepatectomy in animals will result in a critical hypoprothrombinemia which will not respond to the administration of vitamin K.[24]

Patients with primary liver disease or injury may show variable degrees of hypoprothrombinemia This may reach the level at which spontaneous bleeding will occur Most often the prothrombin level parallels the degree of liver injury However, there may be a dissociation of liver functions in patients with hepatocellular disease In some of the most severe cases the prothrombin concentration will remain adequate while a series of liver function tests will show marked abnormalities At other times a case of relatively mild hepatocellular disease as mirrored by a group of tests will show marked hypoprothrombinemia

In all cases of hepatocellular disease there are usually one of three patterns of prothrombin concentration and response to vitamin K therapy

1 A normal prothrombin concentration may be present

2 A low prothrombin concentration may be present which will be elevated by the administration of vitamin K This type of response may occur in relatively mild diseases affecting the liver This response may be temporary and depends more upon general measures aimed at the restitution of all liver functions than to any specific therapy for one dysfunction

3 A low prothrombin concentration may be present which is not elevated by the administration of vitamin K This is the usual response The more severe the hepatocellular disease the more likely is the prothrombin concentration apt to be low and the response to K therapy inadequate

It is often difficult to correlate the type and degree of liver disease with the prothrombin concentration and the response to vitamin K therapy There are exceptions to the rule that a low plasma prothrombin unresponsive to the administration of vitamin K is present in liver disease [25]

Theoretically it is possible to have hypoprothrombinemia in any disease affecting hepatocellular function The most common situations in which the prothrombin concentration is affected at the liver level are acute viral hepatitis, acute toxic hepatitis, acute necrosis of the liver, cirrhosis, leptospirosis icterohemorrhagica, and passive congestion from heart failure

Case V—S R, a 61 year old white housewife, was admitted to the Philadelphia General Hospital October 9, 1948, because of abdominal swelling and exertional dyspnea For forty years her alcoholic intake had been high and her food intake had been low Two years before admission she noted ankle edema, abdominal swelling and weakness These symptoms progressed in severity until

admission Physical examination revealed a dyspneic, edematous patient with numerous spider angiomata over the face and shoulders. There was marked ascites After paracentesis the liver was palpated four fingers below the ribs It was very firm, smooth and not tender The spleen was not felt.

The hemoglobin was 5.2 gm. and the white blood count was 3500 with a normal differential The serum albumin was 1 7 gm and the serum globulin 4 5 gm per 100 cc The serum bilirubin was 1 5 mg per 100 cc, the cephalin-cholesterol flocculation 3 plus in forty-eight hours, the thymol turbidity 8 9 units, and the thymol flocculation 3 plus The serum cholesterol was 90 mg per 100 cc, and the esters were 50 per cent of the total The prothrombin concentration was 24 per cent of normal

She was placed on a high carbohydrate, high protein diet with supplementary vitamins, crude liver extract intramuscularly and ferrous sulfate Three blood transfusions of 500 cc each were given She was given Synkayvite 10 mg three times daily by mouth On November 4 the prothrombin concentration was 35 per cent and on November 15 it was 52 per cent of normal

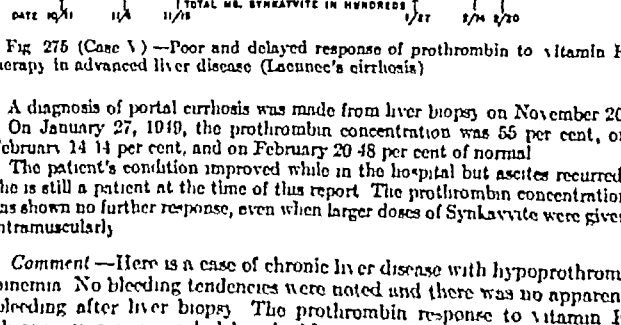

Fig 275 (Case V) —Poor and delayed response of prothrombin to vitamin K therapy in advanced liver disease (Laennec's cirrhosis)

A diagnosis of portal cirrhosis was made from liver biopsy on November 26 On January 27, 1949, the prothrombin concentration was 55 per cent, on February 14 14 per cent, and on February 20 48 per cent of normal

The patient's condition improved while in the hospital but ascites recurred She is still a patient at the time of this report The prothrombin concentration has shown no further response, even when larger doses of Synkavvite were given intramuscularly

Comment —Here is a case of chronic liver disease with hypoprothrombinemia No bleeding tendencies were noted and there was no apparent bleeding after liver biopsy The prothrombin response to vitamin K therapy was poor and delayed After some initial improvement she reached a plateau of concentration which could not be improved by any degree of vitamin K therapy Later there was an actual falling off of prothrombin concentration in spite of continuing therapy Her albumin

deficit was severe and reflects interference with the synthesis of this protein The same interference with the synthesis of prothrombin, unresponsive to K therapy, reflected a failure of this function of the liver

HYPOPROTHROMBINEMIA INDUCED BY THERAPY

Dicumarol, salicylates, quinine, sulfonamides, and streptomycin may decrease the prothrombin concentration by interfering with the metabolism of vitamin K

Dicumarol.—This drug decreases the prothrombin concentration by effectively blocking the action of vitamin K in prothrombin synthesis It does not produce toxic liver injury or interfere with the absorption or bacterial synthesis of vitamin K

The hypoprothrombinemic action of Dicumarol varies in patients, with markedly different rates and degrees of action This does not always depend upon the dose of Dicumarol The difference between a therapeutically useful prothrombin concentration and a critical level is often narrow Bleeding may occur suddenly after what appeared to be a safe level of prothrombin concentration the day before Vitamin K has made the use of Dicumarol practical by providing a readily available antidote

The dose of vitamin K required to neutralize the action of Dicumarol is larger than the ordinary doses given The effective amount of vitamin K administered intravenously may increase the prothrombin concentration within two hours The maximum effect will be obtained in eighteen hours [26] Blood transfusions are necessarily supplied to the patient with bleeding These will supply prothrombin even more rapidly

Recently a comparison was made of the effectiveness of vitamin K_1 oxide, menadione sodium bisulfite and Synkayvite in controlling the hypoprothrombinemia induced by Dicumarol Vitamin K_1 oxide was strikingly more effective in increasing the prothrombin concentration in the shortest time interval The dosage used was larger than that of the other two preparations There were no toxic effects

CASE VI —C M , a 72 year old white male, was admitted to the Philadelphia General Hospital January 24, 1949, with shortness of breath and epigastric pain He appeared acutely ill and was so confused that no history could be obtained Physical examination revealed temperature 98 0, pulse 110, respirations 30 and blood pressure 100/75 He was severely dyspneic, and marked cyanosis was present The thorax was emphysematous and resonant to percussion, with coarse rhonchi and musical rales in both lung fields The heart sounds were inaudible except at the apex There was a soft blowing apical systolic murmur The abdomen was generally distended but peristaltic sounds were normal The rectal examination was negative There was slight pretibial edema

The urinalysis and blood count revealed no significant abnormalities The blood chemistry was normal

An electrocardiogram showed a rapid sinus tachycardia and changes suggestive of a pulmonary embolus There were no signs of myocardial infarction X-ray of the chest reported prominence of the bronchovesicular markings, slight cardiac enlargement and a patchiness with a fluid density obscuring the costophrenic sulcus on the right side

He was given 0 5 gm. of aminophylline intravenously without relief Oxygen therapy was started An initial prothrombin concentration was made and found to be 79 per cent of normal He was given 300 mg of Dicumarol on January 25 On January 26 the prothrombin concentration was 20 per cent and on January 27 it was 15 per cent of normal. No further Dicumarol was given On January 28 he coughed up about one ounce of bright red liquid blood followed by several clots. Six hours later he developed a profuse bloody diarrhea and went into

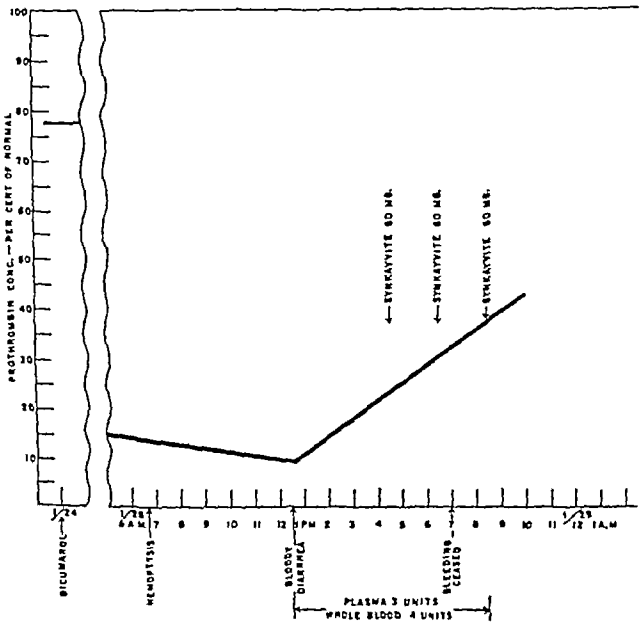

Fig 270 (Case VI) Hypoprothrombinemia induced by Dicumarol and relieved in part by large doses of vitamin K substance

shock Prothrombin concentration at that time was found to be 8 per cent of normal

He was given 2000 cc. of citrated whole blood and 3 units of plasma in a period of twelve hours He was given Synkayvite 60 mg intravenously every two hours for three doses There was no external evidence of bleeding after the second injection of Synkayvite The prothrombin concentration after the third injection was 45 per cent of normal However, the patient failed to respond and died nine hours after bleeding had apparently stopped Permission for autopsy was not obtained.

Comment —This patient developed a critical fall in prothrombin concentration after one standard dose of Dicumarol This reflects the sensi

tivity of some patients to this agent The anticoagulant effect of Dicumarol was being neutralized by the administration of large doses of vitamin K substance, blood and plasma when he died In the majority of cases with this untoward effect of Dicumarol administration, the patient will survive and the anticoagulant can be started again with the same controls Blood transfusions supply prothrombin rapidly but do not inhibit the action of Dicumarol Vitamin K does not supply prothrombin but inhibits the action of Dicumarol by stimulating prothrombin synthesis Its effect is slower but more lasting

Salicylates.—Hypoprothrombinemia may develop during the course of prolonged salicylate administration This reaction is not always related to the dosage of the drug However, it is more frequent after large and continued dosages Patients receiving these amounts should have a prothrombin determination at intervals of a week without bleeding, and immediately and daily when bleeding occurs The action of salicylates in lowering the prothrombin concentration is due to a direct antagonism to vitamin K and resembles the action of Dicumarol

CASE VII —D W , a 12 year old colored female, was admitted to the Philadelphia General Hospital February 13, 1949, with rheumatic fever The present illness had begun eight days before admission with a sore throat Three days later she developed fever and pain in the hip This pain then spread to other joints On admission the temperature was 102 8 There was a Grade I systolic mitral murmur The left knee, right ankle and both elbows were hot, tender and painful on motion

The urinalysis was negative The hemoglobin was 11 9 gm and the white blood count was 22,000, with 90 per cent polymorphonuclears The sedimentation rate was 11 mm per hour Test for sickling was negative

She was given aspirin 20 grains every four hours, and the temperature returned to normal on February 20 The joint pains disappeared more gradually and salicylates were continued in the same dosage

A prothrombin concentration was done on March 1 and found to be 50 per cent of normal She was placed on 20 mg a day of Synkayvite by mouth, and prothrombin concentrations were done every other day There was very little response until about the twelfth day when the concentration rose to 90 per cent This was followed by another drop Parenteral Synkayvite was given twice with a break in the fall and a slow increase in prothrombin concentration

Comment —This patient did not have a critical fall of prothrombin concentration after salicylates Her premedication level was not known Throughout her course she showed moderate reduction of the levels which were relatively resistant to vitamin K administration If she had shown lower levels or had developed any hypoprothrombinemic bleeding, larger doses of vitamin K parenterally would have been indicated. The requirements for treatment of hypoprothrombinemia due to salicylate therapy are similar to those due to Dicumarol therapy

Quinine.—A lowered prothrombin concentration may develop during the administration of quinine salts, and this action may be neutralized by the use of vitamin K A prophylactic oral dose of vitamin K has been

advocated during antimalarial quinine therapy to prevent the hypoprothrombinemia that may result[27]

Sulfonamides—In the preparation of patients for bowel surgery, sulfasuxidine and sulfathalidine are used to reduce the bacterial colony of the bowel This can remove an important source of vitamin K synthesis and, often conditioned by other factors such as decreased intake, diarrhea or liver impairment, hypoprothrombinemia may result Frequent prothrombin determinations are necessary to detect a latent bleeding tendency Vitamin K is administered prophylactically in anticipation of a critical postoperative deficiency

Streptomycin.—The administration of oral streptomycin for intestinal terilization may result in hypoprothrombinemia which is responsive tos the administration of vitamin K

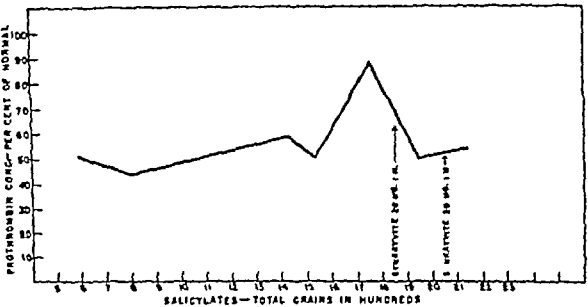

Fig 277 (Case VII)—Salicylate hypoprothrombinemia, showing relative resistance to vitamin K administration

Other Substances—The effect of *penicillin* on the prothrombin concentration is not uniform Recently it was shown that more than 90 per cent of patients in a series showed a decrease in prothrombin concentration while receiving penicillin This effect became evident after only three or four days and disappeared after withdrawal of the antibiotic[28]

Among the manifestations of *aminopterin* toxicity are bleeding gums, skin bleeding and bleeding from the gastrointestinal tract The mechanism of bleeding in these cases has not been determined It is difficult to separate the effects of the disease from the effects of the drug, in evaluation of this phenomenon However, because this *antifolic acid* substance may interfere at some point in the metabolism of vitamin K, it would appear reasonable to watch the *prothrombin concentration* of all patients receiving it

The Response to Vitamin K Test.—If vitamin K is given parenterally to a patient with decreased prothrombin *concentration*, a prompt increase in concentration suggests that the previous low level was due to

either diminished intake or absorption, rather than to liver damage If the prothrombin concentration fails to rise after the parenteral administration of vitamin K, the low concentration is considered to be the result of liver damage No matter how much vitamin K is available, synthesis of prothrombin is impaired within the liver This is the basis of the prothrombin response test of liver function

The correlation between this test and other tests of liver function may be very close [29] However, there may be wide differences between the prothrombin concentration and the severity of liver damage Patients with severe damage as measured by other tests may show a normal prothrombin concentration Mild degrees of liver damage may show marked hypoprothrombinemia [25] In the absence of other factors affecting vitamin K metabolism, failure of the prothrombin concentration to rise after the parenteral administration of vitamin K signifies impairment of this function of the liver It cannot be considered to be a reflection of the general state of the liver This test has the same limitations as any test of liver function The test is useful as an aid in the differential diagnosis of hepatic and posthepatic jaundice but at times it can lead to erroneous conclusions Cases of hepatic jaundice in which the principal derangement is cholangiolar may show a good response and thus suggest posthepatic jaundice

Method —The plasma prothrombin concentration is determined The level must be less than 70 per cent of normal or the test cannot be applied If below this level, 2 mg of menadione is administered intramuscularly A response of 15 per cent or more after forty-eight hours is considered to be a negative test This type of response favors extrahepatic causes for the hypoprothrombinemia

ADMINISTRATION AND TREATMENT

The choice of a preparation is complicated by the large number of substances now available Preparations with K activity, analogues of naturally occurring K, have a more rapid and extended effect on the prothrombin concentration than natural K Modifications of these have the advantage of water-solubility and can be given by mouth without bile salts and intravenously without difficulty

Table 1 is a summary of some of the substances available, with their usual dosage

Synthetic K_1 and K_1 Oxide (K_1 = 2-methyl-3-phytyl-1,4-naphthoquinone).—The synthesis of natural vitamin K_1 has resulted in a dependable agent which can be given over long periods without even a minimal toxic effect The oxide is an improvement over the original synthetic product in that it is not photosensitive and therefore is more stable

GENERAL THERAPEUTIC CONSIDERATIONS

Mode of Administration.—The oral method is satisfactory where a gradual and constant therapeutic response is desired The oral adminis-

tration of natural K and menadione must be accompanied by bile salts in the presence of jaundice Water-soluble preparations do not require their use

Supplementary Therapy —In the presence of hypoprothrombinemic bleeding the addition of blood transfusions is necessary to supply prothrombin at once In the presence of severe hepatic impairment, the

TABLE 1

VITAMIN K PREPARATIONS AND DOSAGES

Name	Available Forms	Average Dose	Bile Salts with Oral Medication in Presence of Jaundice
Kletoyen (natural K concentrate)	Capsules—1000 units	1 capsule t.i.d.	+
Menadione (2 methyl 1 4 naphthoquinone)	Tablets 1 2 mg.	1 or 2 tablets daily	+
Kappaquinone (menadione)	Tablets 1 mg.	1 or 2 tablets repeated each 12 hours as indicated	+
Thioquinone (menadione)	Capsules—1 mg. Vials—10 cc. for oral use Vials—1 cc. for I V use	1 or 2 capsules or 1 2 cc. oral solution daily and repeated as indicated. 1 2 cc. S C or I M	+ (when oral preparations are used)
Hykinone (menadione sodium bisulfite)	Tablets—4.8 mg. Ampules—0.5 cc containing 2.4 mg Ampules—1 0 cc containing 4.8 mg. Ampules—10 0 cc. containing 72.0 mg.	1 tablet repeated in 12 hours as indicated 0.5-1 cc. S.C., or I.M. or I V as indicated. 10 cc. I V as an antidote to Dicumarol	–
Synkavite (tetrasodium salt of diphosphoric acid ester of 2-methyl 1 4 naphthohydroquinone)	Tablets— 5 mg Ampules—1 0 cc. containing 5 mg or 10 mg.	1 tablet repeated in 12 hours as indicated. 1 cc S C., I.M or I V	–
Synkavite (2 methyl-4 amino-1 naphthol hydrochloride)	Capsules—4 mg Ampules—1 cc containing 1 mg.	1 tablet repeated in 12 hours as indicated 1 cc -3 cc. S C I.M or I.V	–

S C., subcutaneously I M. intramuscularly I.V., intravenously

treatment is directed toward its improvement The administration of vitamin K is of secondary importance

SPECIAL THERAPEUTIC CONSIDERATIONS

Table 2 lists the method of administration of vitamin K preparations in specific conditions

The prothrombin concentration must be measured in the preparation of patients for operation who have had chronic intestinal derangements or disease Increased bleeding in ulcerative diseases of the int

require the administration of vitamin K before the usual clinical manifestations of hypoprothrombinemia have appeared

In all patients with biliary obstruction or fistula who have been operated upon, and in whom the initial prothrombin concentrations

TABLE 2

VITAMIN K THERAPY IN SPECIFIC CONDITIONS

Type	Oral	Parenteral	Supplementary
Simple (Idiopathic) K Avitaminosis	1-2 mg menadione once or twice daily	1-2 mg menadione I M. daily	General nutritional therapy Blood transfusions if bleeding
Hypoprothrombinemia of the Newborn	Prophylaxis early in labor 20 mg of water-soluble K substance by mouth	Prophylaxis late in labor 10 mg of water-soluble K substance S C, I M or I V Treatment of infant with hypoprothrombinemia 1 mg water-soluble K substance for first few days	In infant with bleeding blood transfusions, 15 cc. per pound of body weight.
Hypoprothrombinemia of Intestinal Disorders	Parenteral route preferable	1-2 mg menadione S C or I.M or 5-10 mg water-soluble K substance S C, I M, or I V daily	Measurement and treatment of any impairment of hepatic functions Blood transfusions if bleeding
Hypoprothrombinemia of Biliary Obstruction or Fistula	2 mg -4 mg natural vitamin K or menadione with bile salts or 2-10 mg of water-soluble K substance without bile salts daily	2 mg of menadione S C or I.M or 5-10 mg water-soluble K substance S C, I M, or I V daily before operation	Measurement and treatment of any impairment of hepatic functions Relief of obstruction Blood transfusions if bleeding
Hypoprothrombinemia of Liver Disease or Injury	Natural vitamin K or menadione 2 mg daily with bile salts (in absence of jaundice bile salt concentration of bile may be low) or water-soluble K substance 5-10 mg daily	Menadione 2 mg S C or I M or water-soluble K substance 5-10 mg S C, I M, or I V daily	Measurement and treatment of impairment of all hepatic functions Blood transfusions if bleeding
Hypoprothrombinemia induced by Dicumarol Therapy		Water-soluble K substance 60-72 mg I V every 4-24 hours	Withdrawal of Dicumarol Blood transfusions if bleeding.

S C, subcutaneously, I M, intramuscularly, I V, intravenously

were low, it is important that vitamin K therapy be continued for a week postoperatively The danger of bleeding has not been passed often as late as the tenth postoperative day

The hypoprothrombinemia of severe liver disease will not respond to vitamin K. This does not mean that vitamin K should not be given The most important part of treatment is that aimed at recovery of the hepatic lesion Blood transfusions will be needed to correct a critical

development of synthetic substances with K activity They have gradually superseded the administration of the natural vitamin

The prothrombin determination is of clinical importance before operation in patients with jaundice and without jaundice The latter group will include patients with intestinal disorders, hepatocellular impairment, and those who have received agents which suppress the bacterial colony within the intestine

The routine practice of administering Dicumarol to patients with thromboembolic diseases makes an understanding of all of the actions of vitamin K and its administration mandatory The practicability of this practice has been extended by the availability of the antidote to excessive anticoagulant action which is present in vitamin K

Vitamin K is of major clinical importance in medicine, surgery and pediatrics Its usefulness in preventing abnormal bleeding is directly related to this recognition of its important role in the daily practice of medicine

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THE CLINICAL SIGNIFICANCE OF THE INTERRELATION OF NUTRIENT FACTORS

S O Waife, M D *

The practicing clinician is chiefly interested in getting his patient well as quickly as possible This is a complicated process that involves much more than specific therapy, if available He knows that every illness leads to an inadequate intake of food and an increased bodily need for some if not all of the essential nutrients

The pigeon holing of facts which inevitably develops as knowledge accumulates, has, in the case of nutrition, made the doctor think of proteins, fats, carbohydrates, calories, vitamins and minerals as independent building blocks in the total structure of man He may not be aware of newer concepts of human metabolism, a large complex family where everyone is related to everyone else in some way We know from recent work with isotopically tagged molecules[1] that all nutrients enter into a gigantic metabolic pool and there undergo simultaneous transformation and synthesis into a multitude of substances, constantly being broken down and rebuilt again at variable rates of speed and always changing with the needs of body in health and disease, at work and at rest

We intend to show that this intimate interrelation of dietary nutrients speaks against the "specificity" of clinical lesions and that the disturbance in availability of any one vital nutrient affects the optimum function of the organism

VITAMIN A

Let us first consider the ramifications of vitamin A The two physical signs most clearly associated with avitaminosis A are impaired adaptation to darkness and hyperkeratosis However, Stewart[2] reported that daily doses of 150 mg of ascorbic acid produced as great an improvement in dark adaptation as did daily doses of 24,000 I U of vitamin A Furthermore, good adaptation was invariably shown by subjects with a dietary history adequate for vitamins A and C Poor adaptation was associated with a low intake of both of these substances Vitamins A and C are also partially interrelated in that the blood and liver content of ascorbic acid was less than half of normal in experimental vitamin A deficiency, while scorbutic signs could be aggravated by increasing the protein content of the diet in avitaminosis A [3]

Several reports have shown that hyperkeratotic lesion, similar to those

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From the Nutrition Project Philadelphia General Hospital The Nutrition Project is supported by grants in aid from Swift & Co and National Livestock and Meat Institute

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seen in avitaminosis A, may be found in scurvy and niacin deficiency The skin apparently may also reflect a disturbance in fatty acids and pyridoxine If, as has been suggested,[4] pyridoxine is connected with the utilization of unsaturated fatty acids we can see how a single lesion may be the result of an inadequate amount of two or more unrelated nutrients

Vitamin A, furthermore, is partially dependent on vitamin E Adequate hepatic stores of vitamin A require a sufficient intake of vitamin E Curiously, however, cod liver and other fish oils (which contain vitamin A) can destroy vitamin E in the intestines, if fed within a few minutes of each other[5] Here riboflavin enters the picture, for it can counteract this deleterious effect of marine fatty acids under certain conditions

In addition, a number of investigators have shown that in the presence of vitamin A deficiency large doses of vitamin D produced toxic changes which did not occur if adequate amounts of vitamin A were given

Vitamin A also plays a role in protein metabolism It is essential for the growth of tissue (protein) in young rats, but not for its maintenance in adulthood It has been said that vitamin A is held in the liver in the form of a protein complex Alcohol invariably hastened the depletion of hepatic vitamin A stores, probably by lowering the liver component to which the vitamin is attached

It also appears that in patients with cancer an adequate intake of choline is necessary for normal lipid metabolism before vitamin A can be utilized[6] Thus we have seen that vitamin A is directly involved in the metabolism of choline and vitamins C, D and E

THE VITAMIN B GROUP

The literature on the activities of this heterogenous group of essential nutrients is tremendous Only a few points of clinical interest will be mentioned to show the scope and complexity of the effect of one substance on another

Riboflavin deficiency undoubtedly results in cheilosis However, this clinical sign is not "specific" for ariboflavinosis Machella,[7] for example, found improvement in nine of thirteen cases of cheilosis on pyridoxine alone The other four also failed to respond to riboflavin administration In fact, vitamin C produced healing in two cases which had not responded to the entire B complex group

Corneal vascularization may be due to riboflavin deficiency Kruse[8] believes this is specific However, it has been shown that the lesion merely means that at one time a deficiency of riboflavin occurred and trauma such as wind or dust may reactivate its presence This vascularization may be a nonspecific response to a general vitamin deficiency.[10] Similar lesions have been described in experimental deficiencies of vitamin A, tryptophane, lysine, zinc and sodium[11] That the same lesion may be produced by multiple deficiency (Table 1) was further shown by Syden- [illegible] and his associates[12] in rats where corneal vascularization fol-

lowed the lack of any one of the ten essential amino acids as well as pyridoxine and pantothenic acid

Tongue changes have long been considered a specific B complex lesion However, Bakwin and others[13] reported that in a group of sixty children with glossitis and fissures of the tongue even prolonged (as much as two years!) and adequate nicotinamide therapy produced a very slow, irregular response if at all Furthermore, the diets of these children did not differ significantly from those with normal tongues and they concluded that it has not been proved that these common tongue lesions are caused by niacinosis Others[14] also caution against the concept of a typical pellagra glossitis or "riboflavin tongue"

Riboflavin and niacin are essential in the assimilation of protein and in its resynthesis into tissue protein The site of this interaction is probably in the liver, for the hepatic content of those substances was increased by feeding a high protein diet and not by excessive feeding of

TABLE 1

SOME EXAMPLES OF MULTIPLE NUTRIENTS AFFECTING SINGLE TISSUES

(Adapted from Follis[11])

Tissue	May be affected by deficiencies of:
Cornea	Sodium, zinc, tryptophane, lysine, histidine, riboflavin vitamin A
Epidermis	Magnesium, zinc, riboflavin, pantothenic acid, pyridoxine, biotin, vitamin A, linoleic acid
Kidney	Magnesium, potassium, chlorine, choline, linoleic acid
Bone	Calcium, phosphorus, vitamins A and D
Peripheral nerve	Pyridoxine, pantothenic acid, riboflavin?, niacin?

the vitamins themselves Thiamine did not join this group, for it varied directly with its dietary intake[15]

Niacin alone of the B group can alleviate the severity of choline deficiency in rats[16] Many other relationships between these members of the water soluble group exist Thus, in a deficiency of thiamine, riboflavin or vitamin A, but no pyridoxine, there is a reduction in the vitamin C content of tissue[17] Another example is the findings that thiamine and pantothenic acid deficiencies interfere with riboflavin mobilization in the liver[18]

At times, however, the administration of one member may produce a deficiency syndrome This curious finding occurred when six members of the B complex group (thiamine, riboflavin, pyridoxine, niacin, choline and pantothenic acid) were fed with inositol A syndrome developed which could only be prevented by para-aminobenzoic acid, but if para aminobenzoic acid were added to these same six vitamins, inositol deficiency resulted.[19] The explanation apparently lies in the bacterial synthesis of bacteria which will be discussed below

Another finding of clinical importance is that in cases of thiamine deficiency there is a disturbance in riboflavin metabolism, although the

reverse does not hold true Thus, riboflavin deficiency may exist as a result of impaired utilization in the presence of insufficient thiamine as well as a result of an intake insufficient for the body's needs [20]

Pellagra, of course, is known to be a "specific" deficiency disease. For many years the role of corn in the production of pellagra was a puzzle and challenge It was known that aniacinosis may exist in corn eaters even when their diets contained more niacin than in other pellagra-producing diets It was more recently found that niacin and tryptophane are essentially interchangeable Corn protein has a very low tryptophane content and it is believed that pellagra represents a combined niacin and tryptophane deficiency It is now known that pyridoxine (vitamin B_6) is necessary for the conversion of tryptophane to niacin Hence, it is likely that here, too, is an example of either the nonspecificity of nutritional "lesions" or better, the close interrelation of all vital foodstuffs

TABLE 2

VITAMINS AND THE ENZYME SYSTEMS IN WHICH THEY ACT

(Adapted from Knight[16])

Thiamine	Pyruvate decarboxylation and other thiaminoprotein enzymes
Riboflavin	Oxidation of pyridine nucleotide coenzyme, i e , cozymase, D-amino acid oxidase, oxidation of hypoxanthine and certain aldehydes
Nicotinic acid	Dehydrogenases, (di- and tri-phosphopyridine nucleotides)
Pyridoxine	Amino acid decarboxylase, transaminase, tryptophase
Pantothenic acid	Acetylation
Biotin	? CO_2 fixation
Folic acid	?

The type of diet, of course, greatly affects the balance between vitamins A high fat diet may increase the body's need for riboflavin and vitamin E but may spare some nicotinic acid Pantothenic acid deficiency becomes more pronounced on a high carbohydrate diet than on a high fat diet, while if fat is omitted, a pyridoxine deficiency becomes more pronounced Furthermore, the requirements for all members of the B complex group depends on the carbohydrate intake (for their role is predominantly in carbohydrate intermediary metabolism) (Table 2) But not all carbohydrates act similarly Generally speaking, starch, lactose, glucose and sucrose in that order favor intestinal synthesis (vide infra) but that order varies somewhat with specific vitamins [21] Significantly, thiamine synthesis is depressed by rice, which itself is practically devoid of thiamine, and this may explain the prevalence of beriberi in rice-eating regions

VITAMIN C

Ascorbic acid plays a role of many facets in our metabolism While gingivitis is frequently found with lack of this vitamin, it may also be present in deficiency of vitamins A, D and niacin Furthermore, scurvy

exists without gingivitis and gingivitis in otherwise healthy individuals may not respond to ascorbic acid therapy

Vitamin C also favors the absorption of iron by preventing the oxidation of the ferrous form to ferric which is less readily absorbed [22] In addition, vitamin A is related to vitamin C in that the ability of cattle to synthesize vitamin C is reduced in the presence of vitamin A deficiency The clinical value of an adequate vitamin C intake is apparent

Since vitamin C is necessary for the formation and maintenance of intercellular supporting tissues and vitamin D is essential for the calcification of such tissues as growing enamel dentin and alveolar bone, it may be worthwhile digressing to review what we know about that most common of all diseases—dental caries

Dental Caries.—In brief, the progress of dental decay is not influenced by the mineral content of the teeth except for fluoride Careful studies have disproved the concept that caries can be produced or prevented by alteration in vitamin and mineral intake At the most, disturbed calcification such as may occur in rickets can affect the rate of progress of caries, but it is not a factor in its formation

While one would like to think that nutritional deficiencies (therefore amenable to treatment) may cause caries, it is, however, frequently observed[23] that caries occurs in people subsisting on an "optimal" diet and is just as frequently absent in people on a nutritionally deficient diet In fact, it has even been suggested that there is a reduced susceptibility to dental decay in malnourished children [24] At any rate, it is more than likely that the physical nature of the diet is more important than the chemical content

MINERALS

We have emphasized the vitamin problems chiefly because they have commanded a disproportionate segment of the recent investigative spot light Similar interrelations occur with minerals as well and are well known For example, calcium utilization is adversely affected by an excess of magnesium and oxalate in the diet While both calcium and magnesium absorption is favored by a high phosphorus diet (as well as an acid reaction in the intestine), iron and manganese form insoluble phosphate compounds in the bowel and may therefore impair phosphorus absorption [24]

Follis[11] has made the interesting observation that certain myocardial lesions may occur in experimental potassium deficiency, but if there should be a concomitant thiamine deficiency no such lesion appears. Here we see a curious interrelation of vitamin and element in which deficiency of one protects the body from the injurious effect of another nutritional deficiency While the exact significance of these experimental findings is unknown at present, the close interwoven effect of all nutrients is obvious

NUTRIENTS AND IMMUNITY

For at least thirty years, the professional and layman's opinion that nutritional factors are important in resistance to disease has been studied

scientifically Early work showed that vitamins A and D and vitamin "B complex" deficiencies did not impair agglutinin, precipitin or hemolysin formation More recently Cannon and his group[25] have demonstrated the importance of protein metabolism in antibody formation in the experimental animal Our work[26, 27] has elaborated further on this problem in man

We have found that protein deficiency (as indicated by hypoalbuminemia) in man is associated with poor antibody titer levels and low quantitative antibody-nitrogen levels, particularly in the diabetic Protein supplementation in general enhanced the antibody response, but not to levels reached by normoproteinemic patients No relation was noted between the blood sugar and antibody response in diabetics Furthermore, the degree of nitrogen storage (protein repletion) was not reflected in the antibody producing capacity in fourteen subjects [30]

One member of the B complex group may also play a role in antibody formation Axelrod[28] and Stoerck[29] and their co-workers found that pyridoxine deficient rats had an impaired antibody producing ability.

Since antibody is a modified globulin, a protein, studies of the relationship of nutrients and immunity opens new roads to our understanding of many biochemical as well as clinical problems

AMINO ACIDS

Much work has been done on the interrelationships of the essential amino acids For example, it is known that the plasma level of certain amino acids is affected by the feeding of other amino acids [32] Furthermore, Beyer and associates[33] showed that the renal reabsorption of one amino acid is affected by the presence or absence of others Thus, there appeared to be competition for reabsorption between arginine and lysine but not between arginine and glycine; competition between leucine and isoleucine but not between leucine and arginine It is conceivable that excess administration of a single amino acid may have a deleterious effect on tubular reabsorption of other essential protein building blocks

Even the *l* and *d* (optical rotary forms) amino acids seem to compete with each other "for the means by which cells concentrate the amino acids presented them by the extracellular fluid "[34] The absence of a vitamin may affect the urinary excretion of amino acids That is, the excretion of arginine, phenylalanine, tryptophane and histidine, for example, is increased by riboflavin deficiency but unaffected by lack of niacin [35]

Protein Metabolism.—A most significant finding was reported by Geiger[31] and co-workers They showed that all the essential amino acids must be fed *simultaneously* for maximal growth in animals After protein depletion, the increase in weight on re-feeding was retarded if protein and other nutrients were not fed at the same time. Furthermore, cataracts which develop on a tryptophane-deficient diet can be prevented only by feeding that essential amino acid simultaneously with the other amino acids

These reports emphasize the vital necessity of an adequate diet,

adequate in all respects and balanced so that at the same time all essential nutrients can enter the body and be used where they are needed A house is composed of many things and many things must be available at the one time before it can be built

NUTRIENTS AND HORMONES

Like everything else in the body, our amino acids are under the influence of the endocrine glands Friedberg and Greenberg[36] found that plasma amino acid levels were increased by thyroxine and adrenal cortical extract and decreased by insulin, epinephrine, estrogen, thiouracil and hypophysectomy While the exact significance of this observation is not clear at present, it obviously represents an important interrelation of nutrient and hormone which needs further study

Recently, the role of the B complex group of vitamins in estrogen metabolism has been studied It was at first suggested that vitamin B complex deficiency impaired the liver's ability to inactivate estrogen [37] Later it was shown that the concomitant inanition was the chief factor in this effect [38] It now appears that folic acid enables the tissues to respond to estrogen This also has been confirmed by the administration of folic acid antagonists [39]

A recent survey by Samuels[40] collects the wealth of material on the interrelation of nutrients and hormones

VITAMIN IMBALANCE

On the principle that if 1 mg of thiamine is good, 100 mg is 100 times better, many physicians are prescribing excessive quantities of one or several vitamins However, many years ago, it was noted that if thiamine alone were used in the treatment of multiple dietary deficiencies, the symptoms of an acute niacin deficiency may occur, while the administration of niacin alone to pellagrins aggrevated certain signs presumably due to other nutritional deficiencies

Recently it was shown[41] that when patients with pernicious anemia and sprue were treated with folic acid, various signs of vitamin B complex deficiencies appeared only to disappear after liver therapy Here, again, we see the importance of *balance* in the administration of nutrients

ANTIVITAMINS

Essential nutrients are interrelated However, there is a large group of substances called "antivitamins" which are closely related structurally and which may induce specific avitaminoses These metabolic antagonists without specific physiologic activity in themselves apparently interfere with normal metabolic processes by *competitive inhibition* [42]

Awareness of the importance of this concept began in 1940 when Woods and Fildes,[43] and subsequently others showed that para amino benzoic acid, a member of the B complex family, has antisulfonamide activity The chemical structures of these compounds are very similar It was later found that the folic acid molecule contains the para-amino-

benzoic acid structure and that folic acid was essential to the growth of certain bacteria Sulfonamide drugs compete with para-aminobenzoic acid for a place in the folic acid (pteroylglutamic acid) molecule and if they win out are bacteriostatic by preventing the utilization of folic acid (an essential metabolite for certain bacteria) Recent reviews of biological antagonism have appeared to which the interested reader is referred [44]

Antivitamins have been found for vitamins C, E, K and in the B complex group (thiamine, riboflavin, niacin, pantothenic acid, folic acid, pyridoxine, biotin and inositol) Most of these were determined in vitro or in animals Naturally occurring antiniacin and antithiamin compounds have been isolated Woolley[45] has found a nicotinic acid antagonist in corn and it is likely that the frequency of pellagra in certain corn-eating sections of the South may be explained by this factor, in addition to the tryptophane-niacin deficiency discussed before One amino acid has been found to have an antimetabolite analogue, methionine and methoxinine [46]

Avidin is a unique protein found in egg white which combines with biotin to give a complex not broken down during digestion Cooking the egg destroys the biotin-combining power of avidin, and eliminates this antivitamin

A metabolic antagonist of particular clinical importance is that of a coumarin derivative (isolated originally from spoiled sweet clover) which prolongs the prothrombin time by interfering with the function of vitamin K Structurally, vitamin K is very similar to one-half of the symmetrical configuration of Dicumarol *

BIOLOGICAL SYNTHESIS OF ESSENTIAL NUTRIENTS

No discussion of nutritional interrelation would be complete without mention of the lowly intestinal bacteria Their ever-present activities are of definite clinical importance In essence, it appears that certain vitamins can be synthesized (in the presence of an appropriate environment) by the intestinal flora and that others can be destroyed

For example, Young and James[47] found that vitamin C was destroyed by E coli and A aerogenes under both aerobic and anerobic conditions, but in the presence of fermentable carbohydrate (i e , glucose) that vitamin was protected from microbic decomposition [48] From this one can expect that avitaminosis C will occur if insufficient carbohydrate is presented to an intestine harboring a luxuriant growth of these common organisms

On the other hand, folic acid, biotin and para-aminobenzoic acid are synthesized by bacteria as their fecal and urinary excretion often exceeds the intake [49] Moreover, there is experimental evidence that bacterial synthesis of thiamine, riboflavin, niacin and pyridoxine may occur In fact, the presence of relatively insoluble carbohydrates such as dextrin or starch may provide a substrate for added bacterial synthesis of these

* Dr Thompson discusses this in more detail in his paper in this issue

vitamins, for the vitamin requirements of animals was reduced by feeding this type of carbohydrate Another example of the effect of the type of diet on bacterial synthesis of vitamins is the report that a high protein diet tends to suppress riboflavin synthesis, but thiamine synthesis in the intestine is enhanced by dextrose

Even under identical conditions of diet and environment, however, there is a wide variation in the quantities which one individual can synthesize as compared with another Indeed, intestinal bacterial synthesis may reach high levels Thus, Najjar and his co-workers[60] reported that on a riboflavin free diet for over three months no clinical or chemical signs of deficiency occurred in human subjects It is assumed that bacterial synthesis supplied this essential nutrient

Now, it has been shown by many investigators that intestinal bacteriostasis (induced by such sulfonamides as sulfaguanidine and sulfasuxidine) affects bacterial synthesis of certain vitamins particularly of the B complex group, and an otherwise adequate dietary intake may be insufficient if sulfonamide inhibition of vitamin synthesis occurs

Thus, a case of dysentery treated with sulfaguanidine suddenly developed pellagra [61] Apparently this drug disturbed the equilibrium between organisms producing and destroying niacin

In animals, it has been found that sulfaguanidine led to hypoprothrombinemia and that this condition could be prevented by administration of vitamin K, para aminobenzoic acid or folic acid Similar findings were noted with sulfadiazine, sulfathiazole and sulfasuxidine

While we cannot translate these experimental findings to the bedside, the implications should be obvious It would seem that the patient receiving prolonged sulfonamide therapy for intestinal infections should have his nutritional intake adequately supplemented, parenterally, if possible

PERSONALITY AND VITAMINS

A much quoted result of vitamin B deficiency is said to be such phenomena as irritability, fatigue and loss of pep, vim and vigor Such findings have been reported in careful studies by Henderson and his co-workers[62] on the B complex group and by Foltz[63] and others for thiamine Mild depression, lassitude and somnolence has been described in experimental biotin deficiency in man [64]

However the specificity of certain neuropsychiatric symptoms has been questioned by Brill[65] and others Allen,[66] for example, studied 300 consecutive cases with a chief complaint of weakness and fatigue In 80 per cent no physical disorder was found In only one of the 300 cases was vitamin deficiency held responsible for weakness The most frequent physical disorders associated with these symptoms were chronic infections, including tuberculosis diabetes, heart disease, myasthenia gravis and anemia

Fatigability is seen early in the development of pellagra, but it is also seen in almost every illness, while it may be the result of the anorexia

and subsequent nutritional deficiency accompanying a disease it has not yet been proved that it is a characteristic of vitamin B complex deficiency It is certain, however, that thousands of persons in conflict with their mothers-in-law, foremen or spouses are having their irritability and depression treated with vitamins

SUMMARY

This brief review of the highlights of a massive literature on nutritional interrelationships emphasizes two concepts (1) The results of experimental single nutritional deficiencies show widespread effects of metabolic disorders This can readily be understood by remembering the function of vitamins, to mention only one group of nutrients (Table 2) These essential metabolites by virtue of their place in intermediary metabolism directly or indirectly influence every tissue and structure of the body (2) Every nutrient affects and in return is affected by every other nutrient because our body is like a vast city in which the carpenter depends on the cobbler for shoes, and the cobbler on the carpenter for his bench and both on the baker for bread

Clinically, a pure single nutritional deficiency is a theoretical improbability or even impossibility, although such disorders may be predominantly of one type or another The treatment of these deficiencies, whether due to decreased supply or increased demand, or both, involves not only replacement of the primary substance but also the administration of all interrelated nutrients, for each essential metabolite is its brother's keeper

We have seen that certain clinical lesions, formerly said to be "specific" for a nutrient insufficiency, may be caused by several avitaminoses Most vitamins and amino acids are interrelated and one may substitute in part for the other Minerals as well as vitamins are greatly affected by the type of diet consumed

Nutritional factors are affected by hormonal changes and in turn affect the endocrine system Antimetabolites have been discovered and perhaps are important clinically in inducing or aggravating deficiencies Furthermore, bacterial synthesis of vitamins at all times must be considered in the total nutritional picture

Because, for optimal effect, all essential nutrients must be available to the body *at the same time*, all therapeutic considerations must include the time element Excessive and unbalanced administration of vitamins may precipitate other avitaminoses

CONCLUSIONS

Generally speaking, there are no specific lesions caused by single deficiencies and amenable to specific therapy All dietary correction must include the simultaneous administration of adequate amounts of well balanced necessary substances An excess of any one component cannot correct and may worsen the value of the diet as a whole Large doses of vitamins to a patient who is not eating enough calories, carbohydrates

or proteins is as useless in correcting the metabolic disorder as is a diet lacking in essential food factors One can almost describe dietotherapy as "all or none " All nutritional factors in some way are interrelated and optimal results will be obtained if this is remembered

Or to paraphrase old John Donne,—"no nutrient is an island entire in itself "

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RECENT ADVANCES IN NUTRITION

MICHAEL G WOHL, M D, F.A C.P *

Progress in the basic contributions to the science of nutrition has been extensive In this review we shall survey the most notable recent developments in nutrition of practical importance

VITAMIN ANTAGONISTS

The recognition of the existence of vitamin antagonists came largely through the work of Woolley,[1] Woods and Fildes [2] A vitamin antagonist is a structural analogue of a biologically active compound which induces signs of specific deficiency disease The signs of the induced deficiency disease can be nullified by the administration of the biologic compound in question An example is provided by the following a slight modification in structure of nicotinic acid (SO_3 for COOH), results in an antagonistic compound, pyridine-3 sulfonic acid This compound inhibits the growth of certain bacteria The addition of nicotinic acid nullifies the inhibitory effect of the antagonist

Vitamin antagonists have been found in natural occurring forms and many may be synthetically prepared Certain ferns contain antivitamin B_1 [3], certain foods consumed by humans are known also to contain antivitamins of a deleterious nature For instance, raw clams and certain kinds of fish such as carp contain an enzyme that has an antivitamin B_1 activity Fortunately this enzyme is destroyed by heat

Oxythiamine is a thiamine antagonist recently synthesized [4] This compound when given to thiamine-deficient animals may prove fatal Oxythiamine has recently been used in experimental work with polio myelitis virus since the latter is known to develop less rapidly in thiamine-deficient animals It is interesting that mice infected with the virus show less paralysis when they are deficient in tryptophane The possibility of using certain antagonists to modify certain virusss suggests itself [5]

The exact physiologic activity of antivitamin B_1 is not known It may function in a manner similar to other antivitamins (1) by inactivating the specific vitamin (B_1), (2) by uniting with this vitamin forming an irreversible compound and thus render it unavailable (3) it may competitively interfere with the action of thiamine [6]

Some synthetically prepared antivitamins have a chemotherapeutic action Among these are the folic acid antagonists, of which there are

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From the Department of Medicine and the Nutrition Project Philadelphia General Hospital The Nutrition Project is supported by grants in aid from Swift & Co and National Livestock and Meat Institute

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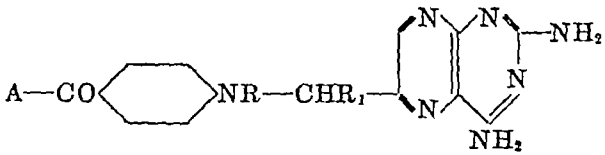
several synthetic preparations [7] One that has aroused considerable interest is *aminopterin* (4-amino-pteroylglutamic acid), which is reported to bring about remission in some children with acute leukemia (see Table 1)

It is interesting to know how the administration of aminopterin in acute leukemia came about Farber[8] observed that the use of folic acid conjugate in leukemia causes an acceleration of the leukemic process in the bone marrow and viscera not seen to that degree in children treated without folic acid Farber felt that it would be worth while to employ this acceleration phenomenon to advantage by irradiation, nitrogen

TABLE 1

4-AMINO-PTEROYLGLUTAMIC ACID AND DERIVATIVES



A	R	R_1	Abbreviated Name	Reference
Glutamic acid	H	H	4-amino pteroylglutamic acid	1
OH	CH_3	H	4-amino-N^{10}-methyl pteroic acid	2
Glutamic acid	CH_3	H	4-amino-N^{10}-methyl pteroylglutamic acid	2
Glutamic acid	CH_3	CH_3	4-amino-9,10-dimethyl pteroylglutamic acid	3
Aspartic acid	H	H	4-amino-pteroylaspartic acid	4

1 Seeger, Smith and Hultquist, J Am Chem Soc *69* 2567, 1947
2 Seeger, Cosulich, Smith and Hultquist, J Am Chem Soc , in press
3 Hultquist, Smith, Seeger, Cosulich and Kuh, J Am Chem Soc in press
4 Mowat and co-workers, in press

(Courtesy of Dr T H Jukes)

mustard therapy or by administration of folic acid antagonists, after pretreatment with folic acid conjugate Indeed, when folic acid antagonist was used by the intramuscular route in fifteen infants and children ill with acute leukemia, ten showed signs of hematologic and clinical improvement It was found at the Children's Hospital of Philadelphia that the drug is superior to blood transfusions, urethane and all other methods employed in the past in acute leukemia in children The recommended dose is 0 5 to 1 0 gm per day intramuscularly It is to be noted that the improvement, although significant, is only temporary [8a] Spontaneous remissions have been known to occur in acute leukemia Aminopterin is toxic and may produce deleterious effects such as stomatitis, spongy gums and gastrointestinal hemorrhages A more potent and less toxic folic acid antagonist, *amino-an-fal*, was recently described

Since folic acid is synthesized in the intestinal tract by certain bac-

teria, it would appear logical to employ a poorly absorbed sulfonamide such as succinylsulfathiozole during therapy with aminopterin Interference with bacterial synthesis of folic acid may enhance the therapeutic effect of aminopterin so that smaller doses may be required in acute leukemia

In recent years other antivitamins have been isolated or synthesized There is at least one antivitamin for each of the water soluble vitamins and for the fat-soluble vitamin K (Dicumarol and derivatives) and E (α-tocopherol quinone) In many instances, there is not one but several antagonists for each biologic compound[9] (Fig 278)

It is interesting to note that antagonists to certain aminoacids have also been described It was shown for example that a compound, indoleacrylic acid, which structurally resembles tryptophane, interferes with the growth of E coli, this inhibitory effect is reversed by the addition of tryptophane[10]

The concept of metabolite antagonism is being actively explored at present by several investigators It may lead to the development of therapeutic agents of practical value

From this brief review, it is apparent that there is a metabolic similarity between all living cells and that biological processes may be blocked by metabolic antagonists

VITAMIN B_{12}

The outstanding contribution in the past year has been the isolation by Rickes[11] and associates from the liver of a crystalline compound, cobalt in nature This compound, B_{12}, in microgram dosage is capable of producing hematopoietic response in patients with pernicious anemia

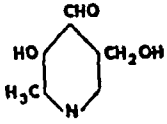
Animal Protein Factor —The discovery of vitamin B_{12} is interwoven with that of the "animal protein factor" In 1946, Cary and his co workers reported that rats require a new unidentified factor that is essential for growth[12] This x factor was found in commercial liver extracts Similar investigations were being carried out by numerous workers They found that the growth of chicks and normal hatchability of hens eggs require in their breeding rations some protein of animal origin Thus, a new nutritional factor designated "animal protein factor" was discovered

Mary Shorb,[13] investigating the nature of the new animal protein factor, found that the microorganism Lactobacillus lactis Dorner required for growth two factors one of these was contained in crude and refined liver extracts She determined that there is an almost linear relationship between the clinical activity of the liver extract in pernicious anemia and the rate of growth of the lactobacillus under study Thus she succeeded in using bacterial growth for assaying liver fractions for antipernicious potency rather than patients, as had been the earlier practice

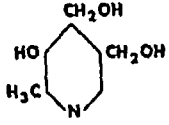
The crystalline substance B_{12} was found to possess growth-stimulating activity in chicks and in Lactobacillus lactis Dorner This suggests the close relationship between B_{12} and the animal protein factor

VITAMINS AND ANTI-VITAMINS

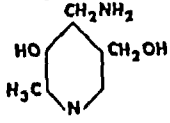
VITAMIN B_6



Pyridoxal

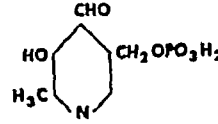


Pyridoxine



Pyridoxamine

all have vitamin B_6 activity When fed, they are partially converted, into

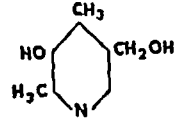


pyridoxal phosphate (co-decarboxylase)

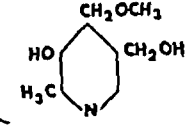
which functions as a necessary part of certain enzymes in

- Tryptophane metabolism
- Amino acid decarboxylation
- Transamination

Some substances such as



4-desoxypyridoxine



4-methoxypyridoxine

because of a structural similarity to the vitamin may inhibit these reactions

SIMILAR RELATIONSHIPS HOLD FOR OTHER MEMBERS OF THE VITAMIN B GROUP

VITAMIN	COENZYME FORM	NECESSARY FOR THE ACTIVITY OF	ANTI-VITAMINS
NIACIN	Coenzyme I, (DPN), coenzyme II, (TPN)	Several Dehydrogenases	Pyridine-3 sulfonic acid 3 acetylpyridine, etc.
THIAMINE	Thiamine Pyrophosphate	Several Organic Acid Decarboxylases	Pyrithiamine 2 butyl thiamine etc.
RIBOFLAVIN	Flavin Phosphate, FAD	Several Oxidative Enzymes	Phenazine analog of riboflavin lsoriboflavin etc.
PANTOTHENIC ACID	Coenzyme A (unknown structure)	Acetylating Enzymes	Pantoyltaurine phenyl pantothenone, etc.
BIOTIN	Coenzyme form not known	Carboxylases, Some Deaminases	Desthiobiotin biotin sulfone etc.
FOLIC ACID	Coenzyme form not known		Pteroylaspartic acid methylfolic acid, etc.

Fig 279--Vitamin B complex, its functions and antagonists (By courtesy of Wayne Umbreight and Gladys Emerson)

It is noteworthy that vitamin B_{12} is synthesized by streptomyces griseus It was isolated from this mold in sufficient quantity to be used successfully in patients with pernicious anemia This may furnish a less expensive source of vitamin B_{12} than the present method of extracting it from liver

Clinical Results.—Vitamin B_{12} is now considered to be the most effective antianemic agent It also produces rapid regeneration of the lingual mucosa Favorable reports on the regression of neurologic manifestations have been reported This is clinically significant since folic acid may correct the blood findings in pernicious anemia in a relapse, but it is generally recognized that the neurologic manifestations are not influenced Indeed, in some instances folic acid may hasten development of neurologic signs and symptoms [14] Patients with nutritional macrocytic anemia of infancy, nontropical sprue and tropical sprue in relapse have shown good hematologic improvement following the use of vitamin B_{12} [15]

At the Philadelphia General Hospital we studied the effects of vitamin B_{12} in eight patients with pernicious anemia, four of whom had neurologic complications [15a] In this paper we are reporting the effects of vitamin B_{12} in three patients with severe forms of pernicious anemia following the intramuscular administration of two doses, each of 25 micrograms of B_{12} at twenty-five day intervals The clinical response was striking All three patients on admission to the hospital were extremely ill, weak, dehydrated, anorexic, and they were mentally depressed Seven days after the first injection, clinical improvement occurred The appetite returned, increasing muscular strength and alertness soon followed Good hemotologic response was obtained in all three patients as illustrated in Figures 279 and 280 *

Report of Case

E R was an 80 year old white woman admitted to the Philadelphia General Hospital (Service of Dr David N Kremer) in January, 1949 because of weakness

Past History Pernicious anemia was first diagnosed in 1945 in this patient at this hospital and treatment with liver extract followed In 1946, she underwent a cholecystectomy for chronic cholecystitis and cholelithiasis In April 1948, one year before this present admission, she again complained of weakness, dizziness, nausea and pain in both legs At that time she was found to be markedly anemic, the liver and spleen were enlarged and there was loss of vibratory and position sense in the lower extremities After a good response to liver, she was again discharged to the Medical Clinic However, she did not attend regularly and had no treatment for about nine months

Interval History The interval history was difficult to obtain on admission because of mental confusion, disorientation and marked deafness She apparently was becoming extremely weak and anorexic

Physical Examination. She was an elderly, extremely pale woman with a blood pressure of 120/60, temperature 100°F, pulse 108, respiration 26 The tongue margins were smooth and although some papillae were found on the dorsum, the

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* We are indebted to Dr Augustus Gibson, of Merck & Co , and C H Mann, of E R Squibb & Sons, for the generous supply of B_{12}

general appearance was that of moderate atrophy There was a moderate tachycardia and a faint apical systolic murmur The liver was just palpable at the costal margin Minimal ankle edema was present The physical examination was otherwise unremarkable.

Neurological Consultation (Dr A M Ornsteen) There are hyperactive deep reflexes but no pathological reflexes Sensation and vibratory senses are within

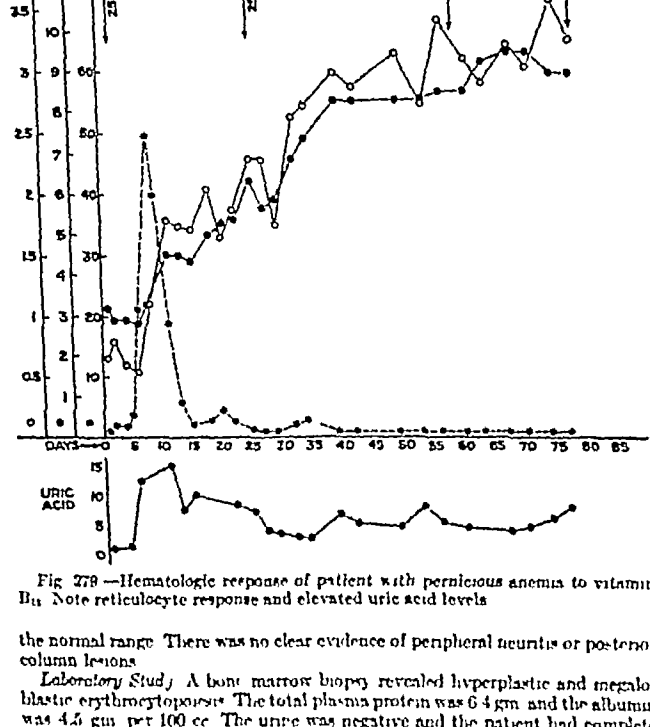

Fig 278 —Hematologic response of patient with pernicious anemia to vitamin B_{12} Note reticulocyte response and elevated uric acid levels

the normal range There was no clear evidence of peripheral neuritis or posterior column lesions

Laboratory Study A bone marrow biopsy revealed hyperplastic and megaloblastic erythrocytopoiesis The total plasma protein was 6 4 gm and the albumin was 4.5 gm per 100 cc The urine was negative and the patient had complete histamine achlorhydria Initial blood count revealed hemoglobin of 3.2 gm and a red cell count of 600,000 per cu mm Two days after the first dose of vitamin B_{12} (25 micrograms) the hemoglobin was 2 95 gm per 100 cc

Course On admission the patient had seemed moribund She was too weak to sit up or feed herself and she was deathly pale By the end of the first week of

therapy, little change was noted Her food intake had been negligible in spite of strong nursing encouragement However, by the second week she began to eat with more interest, she was now able to sit up and there was a slight increase in the papillae of the tongue She progressively became stronger, mentally alert, cheerful and cooperative After two months she was clinically but not hematologically cured During her hospital stay, she received no treatment except ferrous sulfate and vitamin B_{12}

The essential hematologic data are shown in Figure 279

Comment—Several interesting features are to be stressed (1) All three of our cases showed no reticulocytosis upon the second injection of B_{12}, although the red cell count was low enough for one to expect some reticulocyte response (2) The increase in red cells and hemoglobin began to decline at about twenty-five days after the intramuscular injection of 25 micrograms of B_{12} This would suggest that a single large dose of 25 micrograms may suffice in some patients with pernicious anemia for a period of from three to four weeks, however, there is a wide variation in the effective dose in different patients (3) An extremely high uric acid blood level (from 10 to 15 mg per 100 cc) was sustained for fourteen days following the first intramuscular injection of B_{12} This finding was noted in the case cited, in which the patient showed pernicious anemia in the most severe form (Fig 279) (4) The second of our three patients developed hypochromic red blood cells as the maturation of erythrocytes exceeded the available hemoglobin Supplementary oral iron therapy corrected the hypochromia (Fig 280)

AMINO ACIDS

An important phase of protein research has been the development of microbiological methods for the determination of individual amino-acids Such methods, first used for the determination of vitamins, have recently been employed for the quantitative assay of amino acids The "test" microorganisms used in these assays are the species of Lactobacillus, such as Lactobacillus casei, arabinosis, Streptococcus faecalis, and Leuconostoc mesenteroides

We are coming to believe that just as there are vitamin deficiencies of varying degrees, so too there may be amino acid deficiencies It is known that a deficiency of amino acids may develop much more rapidly than a deficiency of vitamins The difficulty has been to recognize specific clinical patterns for amino acid deficiencies in man A few pertinent observations are available Holt and his associates[16] have observed that a few days after subjects are placed on a diet from which lysine has been eliminated, they develop nausea, headache, dizziness, and abnormal sensitivity to noise and excrete nonketogenic organic acids When a casein hydrolysate containing lysine is substituted for the deficient protein hydrolysate, the symptoms disappear, but recur when the deficient hydrolysate is again taken Three subjects on an arginine-deficient diet showed, on the ninth day, alarmingly low figures for spermatozoa When supplementary arginine was supplied, a prompt rise in the sperm count occurred, but only after many weeks of normal diet were normal figures

for spermatozoa restored Holt has reported that, in growing rats put on arginine-deficient diets, marked anatomic changes occurred in the testes as early as the third week The rats' testicular tissue became so dis-

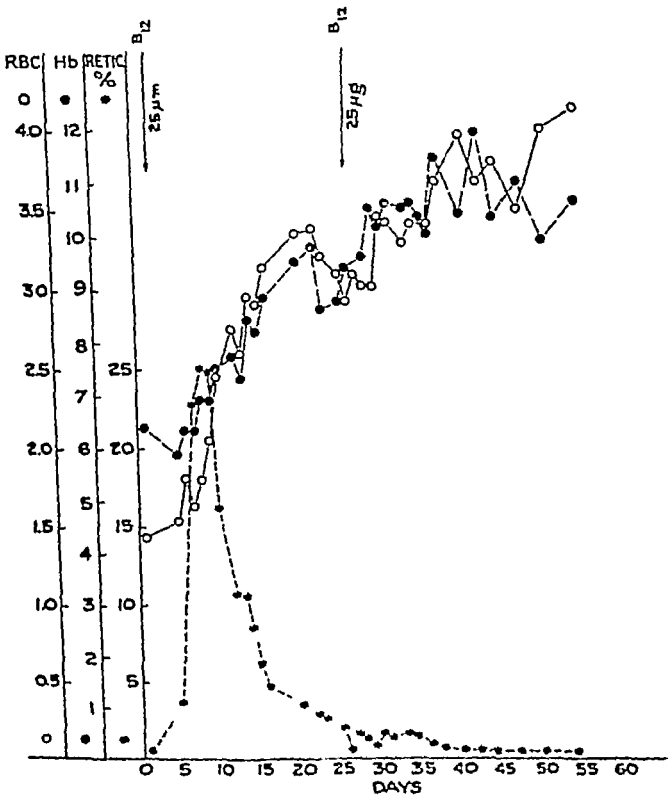

Fig 2-8 —Hematologic response of another patient with pernicious anemia to vitamin B_{12}

organized after two months that it was hardly recognizable, there was no evidence of spermatogenesis and the tubules were filled with cellular debris [11]

With improved methods for estimation of individual amino acids it may be possible to determine whether certain disease states are associated with a specific pattern of amino acid urinary excretion For ex

ample, it is claimed that tryptophane is excreted in greater quantities by the tubercular than by nontubercular patients.

IMMUNITY AND PROTEIN DEFICIENCY

Many diverse factors are involved in the mechanism of immune body formation However, the state of protein tissue reserves plays a significant part in antibody formation

Antibodies are modified plasma globulins The production of antibodies, therefore, in common with globulins, depends upon amino acids in the food or in available tissue protein reserves It would appear therefore that protein deficiency with depletion of protein tissue reserves should lead to lowered capacity to manufacture globulin antibody

Indeed, Cannon and his associates in a series of animals made hypoproteinemic, although well nourished otherwise, have shown that such animals tend to fabricate antibodies less effectively than those whose protein reserves are not depleted Such animals are unusually susceptible to intercurrent infections Thus a simultaneous occurrence of hypoproteinemia and decreased resistance to infection suggests a mutual relationship [18]

Because of practical importance of these findings in human medicine, my colleagues and I have conducted a similar investigation in humans

We investigated two phases of this problem, first, antibody production in hypoproteinemia in man, and secondly, the effect of an increased dietary protein intake in hypoproteinemic patients on the formation of antibodies and other plasma proteins [19]

The method used in this study is interesting By careful survey, over a period of time, a group of patients numbering over one hundred were found on the wards of the Philadelphia General Hospital with hypoproteinemia (i e , less than 4 gm of serum albumin per 100 cc of blood) The hypoproteinemia in these patients was partly due to an inadequate protein intake and was partly a result of their specific disease The clinical ability of the patient to produce antibodies was determined by injecting intradermally 0 2 cc of typhoid antigen and the antibody in the circulating blood was then measured by standard methods

The patients were divided into three groups Group A received the standard hospital diet plus protein supplementation in the form of a protein hydrolysate, group B received a standard hospital diet without supplementation, and group C instead of receiving hydrolysate to supplement the protein intake received a modified casein concentrate preparation Patients were selected in such a way as to keep them clinically comparable to one another The hospital diet provided about 75 gm of protein per day In this connection it is interesting that, in the early period of our studies, we observed that patients failed to respond to the supplementation due to an inadequate protein and caloric intake Thus it became apparent that it was necessary to increase total food intake to prevent weight loss and utilization of the supplemented protein for energy requirements This experience is in line with that of other in-

vestigators who have observed that hospital patients are often on a low intake not only of total calories but of protein

What were the results? Where the patient was able to synthesize protein and the protein reserves were restored upon adequate protein supplementation, antibody formation increased significantly

There was a group of patients in whom the synthesis of protein by the body was markedly impaired (by disease), as, for example, cirrhosis of the liver In these patients the administration of additional protein did not by itself correct the abnormal blood protein pattern Clinical improvement may sometime occur, however, and interestingly enough they showed an increased antibody titer upon supplementation

Another interesting finding arose from this study Supplementation with lactalbumin hydrolysate or casein preparation enhanced antibody formation and partially overcame the subnormal response But the improvement in antibody response failed to attain the high titer observed in subjects with normal blood protein values receiving the same antigenic stimulation This indicates that, other factors being equal, *patients in normal nutritive balance have the best antibody producing capacity* This we believe is a very important point

A relevant phase of our work is that of antibody response in diabetic patients In analyzing a large group of hypoproteinemic patients, we observed, as others have in the past, that the diabetic patient has a decreased capacity to form immune bodies as compared with normal persons We found that the hyperglycemia is apparently not related to the decreased capacity to produce antibodies We further found that, as expected, diabetic patients with hypoproteinemia showed a lower average typhoid agglutination titer than those diabetics with normal blood protein values Thus the lower antibody level in the circulating blood may partly be responsible for the recognized susceptibility of diabetics to infection Supplementation of these hypoproteinemic diabetic patients with lactalbumin hydrolysate or casein concentrate, as in our previously discussed groups, also enhanced antibody formation[22] (Fig 281)

Our work in patients tends to confirm the findings in animals that protein depletion leads to a lessened capacity to form antibodies Furthermore, our experience with diabetics is in line with that of Schneider[23] that patients with complications (hemorrhagic retinitis) show low plasma albumin levels In some patients in whom they succeeded in correcting the plasma protein pattern by high protein diet, retinal hemorrhages were either eliminated or lessened Thus the treatment of diabetic retinopathy by high protein diet seems to hold some promise It is surprising how often in our routine laboratory work up of the diabetic patient with complications hypoproteinemia is uncovered

It is now recognized that in time of stress larger quantities of amino acids should be made available in order to counteract the catabolic loss of nitrogen[24] Surgeons have recognized this and are maintaining the surgical patient on high protein levels

In the management of diabetes this rule has been generally neglected

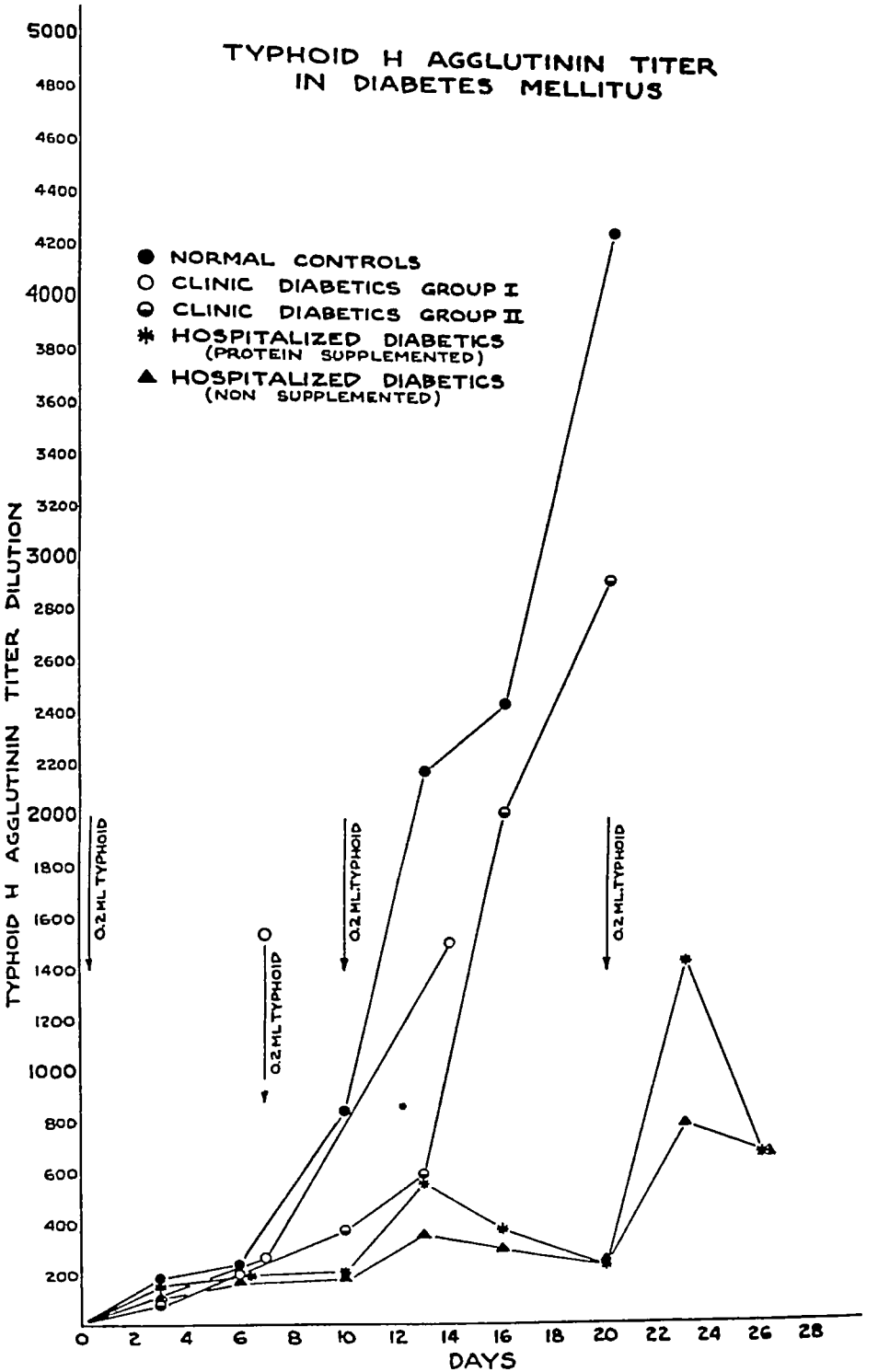

Fig 281 —Antibody response to typhoid H antigen in patients with diabetes mellitus Note the difference between normal controls and hypoproteinemic hospitalized diabetics (Wohl, M G , Proc Soc Exper Biol & Med , Vol 70)

The uncomplicated diabetic patient may do well on the usual food allowance of 60 to 80 gm of protein daily, however, we believe this ration is far too small an amount for the diabetic patient in times of stress due to surgical complications

It is recommended that values of serum protein be determined in every case of diabetes with complications and a high protein diet or protein supplement be given on indication

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CLINICS ON OTHER SUBJECTS

HEART DISEASE AND PREGNANCY

GEORGE E MARK, JR, M.D, F A C P *

One important and vital problem that we as physicians must face from time to time is that of heart disease complicated by pregnancy Sir James Mackenzie[1] has said "there are few subjects in Medicine of which an accurate knowledge is more urgently required than that of a woman's fitness for child bearing"

The main problem facing the physician is that of prognosis Should a given cardiac patient become pregnant or if pregnant should she be permitted to continue her pregnancy? What can one expect during pregnancy, delivery and the postpartum period in reference to the cardiovascular system? The opinion and management of such a problem, of course, will be to a great extent an individual one There have been, however, certain criteria developed which one might use as a guide and which have definitely aided in the reduction of maternal and fetal mortality These will be developed during the course of this paper

PHYSIOLOGY

Successful management of heart disease and pregnancy depends primarily on the attending physician's knowledge of the physiology of normal pregnancy in relationship to the cardiovascular system Cohen and Thomson[2] and Burwell[3] have reviewed the subject and added to our knowledge of these physiological changes during pregnancy At the present time there is evidence that beginning about the second trimester of pregnancy there is a gradual increase in the total blood volume (1 liter), cardiac output (25 to 30 per cent), and heart work (50 per cent) These gradual increases reach a peak at about the thirty sixth week and then there is a gradual drop during the last lunar month of pregnancy Other physiological changes to be appreciated are an increase in oxygen consumption (15 to 20 per cent) during pregnancy and particularly during labor,[4] and a decrease in auricular ventricular oxygen difference There have been various opinions in the past concerning venous pressure, arterial pressure and circulation time during pregnancy More recent studies[5, 6] on venous pressure confirm the generally held opinion that the antecubital venous pressure is not significantly different from that in the nonpregnant state Also that the femoral venous pressure begins to rise in the early part of the second trimester, rises rapidly

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between the twentieth and thirtieth weeks, and then slowly to delivery, afterward falling quickly Circulation time increases somewhat during pregnancy but remains within normal limits Manchester and Loube[6] in a relatively recent report expressed the opinion that circulation time values in the upper limits of normal may in a pregnant cardiac patient be significant of early decompensation, particularly if there were previous comparable circulation times which were shorter It is felt that the arterial blood pressure remains normal with possibly a slight drop in the diastolic pressure, giving a slight increase in pulse pressure as pregnancy progresses There has been some disagreement concerning vital capacity during the normal pregnant state Burwell and his associates[3] and the author have found the vital capacity to show only minor fluctuations

SIGNS AND SYMPTOMS SUGGESTING CARDIOVASCULAR DISEASE

There are certain symptoms and signs suggesting cardiovascular disease which may be a part of the normal pregnancy In a study of 3000 normal pregnant women by Cohen and Thomson[2] the following symptoms were found dyspnea, orthopnea, pseudoparoxysmal nocturnal dyspnea, and palpitation Summarizing their examinations they found a questionable increase in heart size, loud mitral first sounds, and apical systolic murmurs in 50 per cent of the cases, third heart sounds, a P_2 greater than A_2, pulmonary systolic murmurs (100 per cent) tachycardia, extrasystoles, prominent veins, Corrigan-like pulses, capillary pulses, and dependent edema of the legs One can see from these findings that there may be times when it will be difficult to properly evaluate a given case This may be especially true when, as occasionally happens, there is some exaggeration of the normal symptomatology Sodeman[7] has pointed this out and has used the term "gestatory heart disease" for this group Comment might be made at this time on the questionable increase in heart size It is now generally felt that the heart during pregnancy does not enlarge and that the "apparent" enlargement is due to the elevated diaphragms with altered position of the heart

TYPES OF HEART DISEASE

Of the various etiologic types of heart disease to be found in pregnant women, rheumatic heart disease is, as might be expected in this age group, the greatest offender It is found in 90 to 95 per cent of all obstetrical cardiacs The remaining cases will fall into categories such as congenital, hypertensive, syphilitic and kyphoscoliotic heart disease Because of the high incidence of rheumatic heart disease in this group of patients this paper is limited to this type

PROGNOSIS

As a basis for prognosis and evaluation various approaches have been used It may be worth while here again to emphasize that the evaluation of pregnant cardiacs is still an individual one One can, however, make

use of statistics as a guide in the evaluation of a case and that they are of value has been shown by the lowered maternal and fetal mortalities as compared with mortalities fifteen or twenty years ago

The majority of recent authors make use of the New York Heart Association *functional classification*

Class I	Patients with cardiac disease and no limitation of physical activity
Class II	Patients with cardiac disease and slight limitation of physical activity
Class III	Patients with cardiac disease and marked limitation of activity
Class IV	Patients with cardiac disease who are unable to carry on any physical activity without discomfort

Where this classification is used it will be found that approximately 80 to 85 per cent of cardiac patients will fall into Classes I and II About 10 per cent will fall into Class III and the rest in Class IV The majority of Class I and Class II patients will go through pregnancy and labor without any serious cardiac difficulty Class III and Class IV patients are the real problems and it is among them that the greatest morbidity and mortality will occur The proper functional classification of the cardiac patient is the necessary start in our evaluation It must be appreciated, however, that this functional classification may change at any time and if it does, that in itself may be of grave significance

Hamilton[8, 9] has objected to a given standard classification and feels that pregnant cardiac patients fall naturally into three groups Group I are those pregnant women who have unmistakable evidence of heart disease He subdivides this general group into a favorable group and an unfavorable group The favorable group consists of those cardiacs who show evidence of definite heart enlargement and a diastolic murmur This group had an over-all mortality of 2 to 3 per cent The unfavorable group consists of those cardiacs who have signs of/or a history of heart failure, and a dangerous disorder of the heart beat (auricular fibrillation) Hamilton also felt that those patients who develop signs and symptoms of acute rheumatic fever should be included in this group His general mortality rate for the unfavorable cases was 17 6 per cent Group II includes the doubtful cardiacs who show troublesome signs such as a systolic murmur, widened transverse diameter of the heart, increased hilar markings, and a third heart sound at the apex Group III consists of those patients who show no evidence of heart damage but have symptomatic evidence of cardiac neuroses

In the evaluation of a pregnant cardiac patient as to prognosis there are additional points which may amplify or add to those already mentioned These have recently been emphasized by Bunim and Rubricius[10] and are based on the work of Cohn and Lingg[11, 12] and refer to the determination of where in the course of the natural history of rheumatic heart disease the individual belongs It is felt[10, 12] that pregnancy of itself does not alter the course of rheumatic heart disease or shorten the life of the patient The complications which may arise in Class I or II patients may be explainable for the most part by the recognition of

where in the natural history of the disease the case lies In the group reported by Bunim and Rubricius[10] those patients who suffered heart failure had evidence of rheumatic heart disease for an average of seventeen years They show that the incidence of failure increases in proportion to the duration of the cardiac damage. Thus those women who had rheumatic heart disease for less than ten years developed heart failure in only 4 per cent as compared with those having evidence of rheumatic heart disease for more than fifteen years in whom 18 per cent or more failed Such considerations also probably explain statistics as exemplified by Gorenberg [14] In his rather large series he found that failure occurred in 42 6 per cent of pregnant cardiacs over 30 years of age while the rate under the age of 30 years was only 16 1 per cent It has been shown[8, 10, 14] that, of those who had a history of heart failure in the past, 75 per cent had a recurrence of their failure Those patients having auricular fibrillation had a mortality rate of about 33⅓ per cent It is felt[10] that auricular fibrillation is not dangerous because of the arrythmia or therapeutic difficulties but because the patient has reached an advanced stage in her disease

Heart size has been used in the evaluation of these cases and it has been noted that a heart which has enlarged over 10 per cent of normal has a greater chance of failure The type or types of valvular lesions have been commented upon It has been felt that single valvular involvement was less serious than involvement of two valves Bunim and Rubricius,[10] however, opposed this view and showed that failure occurred in 24 per cent of their cases of mitral valvular disease alone but in only 11 per cent of their cases of combined mitral and aortic valvular disease

In view of the fact that the increasing cardiovascular load of pregnancy begins to diminish in the last lunar month, it might be expected that the majority of cases of failure will occur prior to this time In the majority of reported cases the greatest incidence of failure occurred in the seventh and eighth months An exception to this experience has been noted by Bunim and Rubricius[10] who reported that the majority of their failures occurred in the last lunar month

There is one type of cardiac disorder which may be unpredictable and that is mitral stenosis These cases, particularly when accompanied by normal sinus rhythm, may be accompanied by bouts of pulmonary edema It is felt that in these cases there is no drop in the physiological load of pregnancy until delivery and it is not uncommon to find them going into failure immediately after delivery This may occur in spite of a negative past history of cardiovascular embarrassment during pregnancy

FAILURE AT DELIVERY AND DURING THE POSTPARTUM PERIOD

In terms of fatality and congestive failure, the early puerperium is often a most critical time for patients with serious heart disease It has been shown[4, 16] by oxygen consumption studies that the work of labor is variable but often severe and that the load imposed on the heart at

this time may be of significant importance It is estimated by these investigators that work may be performed during labor which is equivalent to climbing a 7 foot flight of stairs once every three minutes during a labor lasting twelve hours Furthermore, the "oxygen debt" incurred during a long and hard second stage may not be repaired for over an hour after delivery This situation is at times reflected by changes in the pulse and the respiratory rate[14] during this period of time It has been noted[14] that 50 per cent of the cases which show, during the first stage of labor, a pulse rate of 110 per minute or more and a respiratory rate of 24 per minute or more for over forty-five minutes will end in failure Mendelson and Pardee[15] feel that if this circumstance occurs the patient should be rapidly digitalized and the second stage of labor eliminated

There is also statistical evidence[17, 18] that the emptying of the uterus may in itself impose a burden on the heart Deaths from congestive failure occur with equal or greater frequency in patients with serious heart disease after cesarean section, where the work is excluded, than after vaginal delivery The physiological reasons for this "placental factor," as a factor in congestive failure, are not too clear at the present time Burwell[8] has likened the placenta to an arteriovenous aneurysm and it has been felt that when this shunt (placenta) is suddenly removed, the over all resistence in the circulation is increased thus placing an added burden on the heart Associated with this thought there is evidence to show, as recently indicated by Brown and her associates,[19] that there is a decrease in vital capacity in the early puerperium followed later by an increase They feel that this is probably due to mechanical factors affecting ventilation rather than to circulatory embarrassment They also found an increase in venous pressure but did not find it at the same time as other signs of cardiovascular embarrassment such as tachycardia, decreased vital capacity and increased circulation time It is believed, however, that the major factor in the precipitation of failure in cesarean delivery is the sudden removal of the shunt and the increased load on the circulation It is suggested that the decreased incidence of failure with delivery by the vaginal route is due to the circulation becoming accustomed to the loss of the placenta by the contractions of the uterus during the early stages of labor More work must be done concerning this problem

Another factor in postpartum failure is based on the work of Albers[20] who described an early postpartum decrease in blood volume followed by an increased hemodilution just prior to the postpartum diuresis Brown and her co workers[19] found that this occurred in their series in the first week of the puerperium and believed it to be partly the result of reabsorption of fluid lost to the tissues during labor, but conceivably could be related to the process of removal of extracellular water during the period of negative sodium balance and diuresis Thus again this secondary hemodilution and increased blood volume of this period may be a factor in initiating failure in a group of patients

One other consideration must not be overlooked in evaluating failure in the postpartum period and that is acute rheumatic fever McKeown[21] reports two patients who had been perfectly well throughout pregnancy but who collapsed and died after delivery In both instances evidence of acute rheumatic endocarditis and myocarditis was found microscopically He thus believed that it was dangerous to correlate the presence of a chronic valvular lesion with fatal outcome in the absence of microscopic examination of the heart

CONTRAINDICATIONS TO PREGNANCY IN HEART DISEASE

Contraindications to pregnancy will again depend in the main on the individual case All of us who have had experience with the pregnant patient with heart disease can cite instances where one has surprised us somewhat and gone through pregnancy, delivery and the postpartum period with relatively little trouble As a group, however, the patients with a past history of failure, with failure in the first trimester of pregnancy, with evidence of auricular fibrillation, and with acute rheumatic fever have a high mortality rate and are considered unsuitable for pregnancy There are patients, however, who, after being informed of the high mortality rate, are still willing to take the risk of pregnancy because of the great desire to have a child They must be permitted to do so Others for religious or varied reasons will not wish to interfere in any way with pregnancy

MANAGEMENT AND TREATMENT

The general obstetrical mortality rate is a fraction of 1 per cent The over-all average mortality of pregnant cardiac patients is approximately 10 per cent Because of the additional risk of pregnancy in cardiac women, they should be followed with additional care preferably by those who are experienced in the handling of this particular problem That this particular point is important is rather dramatically demonstrated by Gorenberg[14] and Stromme and Kuder[21] The former reported 157 obstetrical cardiac patients registered in the clinic, eleven who did not register at the hospital until labor began or who were found to be in cardiac failure at their first antepartum visit, and fifty-five private patients It was to be noted that 54 5 per cent of the nonclinic patients went into failure, 34 5 per cent of the private patients failed, while only 2 5 per cent of the clinic patients failed Death occurred in 18 2 per cent of the nonclinic patients, 9 1 per cent of the private cases, and only 0 64 per cent of the clinic patients The latter authors reported sixty-five unregistered patients with five deaths or a 7 69 per cent mortality rate as compared with 655 registered patients with seven deaths or a 1 07 per cent mortality rate Thus one cannot overlook the fact that probably the main factors in the successful management of these cases is seeing them as early in their pregnancy as possible and making careful and thorough follow-ups

It is my feeling that Class I and Class II patients should be seen by the internist or cardiologist at at least monthly intervals Class IV patients should be hospitalized at the first visit and kept at bed rest during the remainder of the pregnancy All other cardiac patients should have one to two hours of rest during the day and a minimum of nine hours bed rest at night One should be aware that the functional status of any cardiac patient may change Thus if a Class I or II patient becomes a Class III patient during the pregnant state she should be hospitalized and kept at rest for the remainder of her pregnancy During the seventh and eighth months Class I and II patients should be seen at least at two week intervals

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SUMMARY

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SOME KINDS OF HYPERTENSION WHICH DEMAND SURGERY

FRANCIS R MANLOVE, M.D *

So much has been written on the various medical and surgical therapies for "hypertension" that it seems appropriate to emphasize the diagnostic features of certain kinds of hypertension which demand surgery Although rare, as compared to essential hypertension, their importance lies in the fact that timely diagnosis and treatment offer a good chance for cure

Five conditions have been selected pheochromocytoma, Cushing's syndrome, coarctation of the aorta, hyperthyroidism and arteriovenous fistula The problem of renal disease and its relation to the problem of hypertension is purposely omitted

PHEOCHROMOCYTOMA

These tumors arise in the chromaffin tissue of the adrenal medulla or the paraganglia of the sympathetic nervous system Cure of hypertension by operative removal of pheochromocytomas has been reported with increasing frequency during recent years Excellent compilations of this material are available[6, 16, 20, 44]

Pheochromocytomas may occur anywhere in the abdomen, occasionally in the chest,[18] and may be single or multiple[9, 10] They are usually benign but may be malignant[16]

Sex incidence is equal They may occur at any age but are most com
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Sex incidence is equal They may occur at any age but are most common in the fifth decade

Symptoms are produced by the secretion of a pressor substance which is generally agreed to be epinephrine

Symptoms.—Hypertension is the outstanding feature of the disease It may be paroxysmal or sustained The patient may exhibit numerous and striking symptoms and signs or may exhibit only those commonly seen in essential hypertension [20, 49]

PAROXYSMAL HYPERTENSION —Many of these patients have symptoms which one would expect to see following the injection of a large dose of epinephrine At irregular intervals the patient is suddenly seized with tremendous apprehension, headache, tremulousness, nausea and vomiting Dyspnea, palpitations, precordial and epigastric pain, cramps in the extremities and urinary frequency are common Vasomotor phenomena are usually present The skin becomes blanched and cold or it may show alternate blanching and flushing Raynaud's phenomenon has been described During the attack there may be drenching, paroxysmal sweats

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Physical examination reveals elevation of both the systolic and diastolic blood pressures to levels which may be alarming The systolic pressure is usually above 200 mm of mercury Between attacks the pressure falls to or near to normal The neck, during a paroxysm, enlarges and its veins become engorged A pronounced tachycardia is usually present but bradycardia may supervene Extrasystoles are frequent Pulmonary edema appears, during the attack, in about one-half of the cases [24] In half the cases, examination of the abdomen will reveal either a palpable tumor or a kidney or liver displaced by the tumor

Laboratory Examination—Hyperglycemia and glycosuria are frequent but not constant findings These result from glycogenolysis induced by adrenalin The urine frequently contains albumin and casts The blood urea clearance may be decreased or increased [36] The electrocardiogram frequently reveals disturbances of rhythm auricular and ventricular tachycardia, ventricular extrasystoles or the appearance of nodal rhythm [24, 35] The last is probably a vagus response During the paroxysm the T waves may become elevated

Precipitating Factors—An attack may be induced by any activity which mechanically stimulates the tumor physical effort, bending or twisting, or palpation of the abdomen With hyperventilation, descent of the diaphragm may mechanically stimulate a tumor which lies immediately beneath it This is probably the mechanism where paroxysms are induced by emotional upsets Either fasting or overeating may induce attacks And finally, there often is no discernible precipitating factor

Chronic Hypertension An increasing number of cases are reported which fall into this category Pheochromocytoma should be suspected in any patient who exhibits the triad hypertension, hyperglycemia and hypermetabolism The usual symptoms of pheochromocytoma may be entirely absent[49] and the tumor discovered during exploration for sympathectomy [11] There is persistent elevation of both the systolic and diastolic blood pressures The optic fundi show varying degrees of change ranging in severity up to the retinopathy of malignant hypertension Thus, the full-blown picture of malignant hypertension may appear and death from renal failure may ensue [22] Cardiac hypertrophy occurs frequently and the electrocardiogram may show the pattern of left ventricular strain

Laboratory Findings—The basal metabolic rate is often elevated and, in fact, the condition has been mistaken for hyperthyroidism [36] Frequently there is hyperglycemia with glycosuria or at least a diabetic glucose tolerance curve The hyperglycemia is difficult to control with insulin In some instances, prolonged hyperglycemia appears to cause lasting damage to the pancreatic islets [15, 19] Severe diabetic acidosis is not reported

Diagnosis.—1 *Blood pressure* should be recorded frequently It is desirable to record the blood pressure every hour for a twenty-four hour period in order to determine the presence or absence of fluctuation

2 *Pyelograms* may reveal the shadow of a tumor mass or may show displacement of a kidney.

3 *Tests which precipitate an attack of paroxysmal hypertension*

(a) Mechanical stimulation of the tumor by massage of the abdomen, bending or twisting the trunk, or hyperventilation
(b) Histamine test [9] Histamine base 0 05 mg is injected intravenously In the patient with a pheochromocytoma, the injection is promptly followed by a striking rise in blood pressure accompanied by the typical symptoms of an attack. No such response occurs in normotensives or in persons with essential hypertension.
(c) Tetraethylammonium bromide has been used successfully in one case [11] The intravenous injection of 400 mg promptly induced an attack. This drug had the advantage, because of the sympathiolytic effect, that when the blood pressure rose to alarming levels it could be reduced by having the patient sit or stand up

4 *Adrenolytic Drugs*—In the patient with a pheochromocytoma, these drugs produce a fall in blood pressure by destroying epinephrine which is circulating in the blood They are especially useful in the evaluation of the patient with chronic hypertension A number of adrenolytic drugs have been produced Two benzodioxanes, 933F and 1164F, have been tried 933F appears to be the better [9, 16] The dose is 0 25 micrograms per kilogram of body weight given intravenously At this dosage level the drug is adrenolytic, larger doses are sympatholytic When the injection is timed to take two minutes, side reactions are not troublesome The injection is followed by a prompt, temporary fall in both the systolic and diastolic blood pressures Normal subjects show a mild pressor response while patients with essential hypertension show a slight, brief fall in blood pressure followed by a pressor response

5 Tests which are of questionable value or which should not be used

(a) The injection of epinephrine may be followed by an attack. On the other hand, the patient may be abnormally insensitive to it [11, 15]
(b) Acetylcholine has been used to induce attacks but is considered dangerous [9]
(c) Carotid sinus pressure may or may not induce an attack.
(d) X ray following perirenal insufflation of a gas should not be used The test entails some danger in the best of hands and these patients are notoriously bad surgical risks There is the additional factor that the tumor may be extra-adrenal and would not be visualized anyway

Prognosis.—The major causes of death in untreated cases are acute left ventricular failure, chronic congestive failure, or a cerebrovascular accident Sudden death or death during a minor surgical procedure may occur or there may be progressive renal failure with death in uremia

Case I —*Pheochromocytoma of Right Adrenal Gland*—I E., a white man aged 54, was admitted to the Philadelphia General Hospital on March 20, 1947 He had been well until two days ago when he experienced a sudden attack of severe headache weakness and vertigo and fell down the stairs He immediately felt excruciating pain in his right hip and was unable to move the right leg

Past medical history revealed that the patient had been told five years ago, that he had high blood pressure Two and one-half years ago he had had a "stroke" involving the right side

Systemic review revealed that he had frequently been subject to tachycardia, palpitations and dyspnea He passed urine five or six times daily and once a night

The significant physical findings were systolic blood pressure 220 mm of mercury, diastolic 140 mm The palpebral fissures were wide suggesting exophthalmos Optic fundi showed "mild hypertensive changes" The point of maximum impulse was 1 cm to the left of the midclavicular line in the sixth interspace There was a blowing systolic precordial murmur heard best at the apex The right leg was shortened and externally rotated

Laboratory Findings The urine contained albumin 3 plus and a few granular casts Fasting blood sugar was 96 mg per 100 cc and the blood urea nitrogen was 22 mg per 100 cc Basal metabolic rate was plus 24 per cent X-ray of the right hip revealed an intertrochanteric fracture

On March 1 a bilateral saphenous ligation was done and on March 27 the hip was pinned

The patient's course, following surgery, was marked by continued low grade fever, apathy, profound sweats and fluctuation of the blood pressure between 200 and 250 mm of mercury systolic and 100 and 180 mm diastolic Bouts of cardiac arrhythmia occurred simple tachycardia, auricular extrasystoles and one bout of paroxysmal auricular fibrillation

On May 5 the patient suddenly expired An autopsy revealed a pheochromocytoma of the right adrenal gland There were multiple areas of hemorrhage and scarring throughout the brain

CUSHING'S SYNDROME

Cushing's syndrome is characterized by hypertension, diabetes, obesity, osteoporosis, certain changes in the skin, muscular weakness, hirsutism, amenorrhea and loss of libido These all appear due to adrenal cortical hyperfunction [1] The syndrome has been correlated with benign and malignant tumors of the adrenal cortex, adrenal cortical hyperplasia and basophil adenomas of the pituitary Adrenal cortical hyperplasia may or may not be accompanied by a basophil adenoma of the pituitary, and it should be noted that this syndrome has occurred in the absence of any demonstrable abnormality of the endocrine glands There is not space here for a lengthy discussion of the many variations in this syndrome, its relation to the adrenogenital syndrome, or the complex endocrine interrelations The interested reader is referred to excellent reviews of this problem which are available [2, 26, 44 48]

Clinical Manifestations.—Hypertension is almost always present with elevation of both the systolic and diastolic pressures The hypertension may be mild or it may be so severe as to exhibit the optic, cardiovascular and renal features of malignant hypertension [44]

The diabetes is characteristically mild and may be merely demonstrable as such It is due to the excessive conversion of protein into glucose and is markedly resistant to insulin [1]

Obesity is more apparent than real It is confined to the upper half of the body, producing a typical "moon face" and pads of fat over the upper back and shoulders causing a "buffalo hump" appearance The abdomen is protuberant not so much from obesity as from relaxation of the muscles of the wall and kyphosis secondary to collapse of vertebrae

Osteoporosis is found in most cases and is thought to be due to failure of bone matrix formation secondary to protein destruction It is most commonly found in the skull, spine and ribs The pain caused by vertebral collapse may be a prominent symptom

In contrast to the obesity is the actual loss of muscle mass from the extremities and its accompanying muscular weakness

The skin, by its atrophy and increased transparency, acquires a characteristic reddish hue Purple striae are seen, especially over the abdomen, flanks and buttocks These are not to be confused with the white striae commonly seen on normal people These people bruise easily Acne is common

Among women hirsutism and amenorrhea may appear Loss of libido occurs in both sexes

Laboratory Examination

1 *X-ray*

(a) Of bones for osteoporosis[a]
  (1) The frontal and parietal bones of the skull show circumscribed, irregular areas of rarefaction which may resemble tumor metastases
  (2) The entire spine shows uniform decalcification which may be mild, or severe and complicated by compression fractures. The bony trabeculae are decreased in number and density
  (3) Enlargement of the rib ends at the costochondral junctions occurs resembling callus
(b) Pyelograms may reveal displacement of the kidney by a tumor or the presence of a tumor above the kidney
(c) Perirenal insufflation of air may be needed to demonstrate the presence of adrenal hyperplasia The procedure may have to be used despite its danger
(d) X ray may show enlargement of the sella turcica when a basophil adenoma is present but this is not always so
(e) X ray of the chest to rule out thymic tumor should be done

2 *Hormone studies* are useful when available In Cushing's syndrome due to adrenal cortical tumors there is usually increased excretion of urinary androgens and estrogens This change is absent when the syndrome is not due to tumor

3 *Fasting blood sugar* and perhaps the *glucose tolerance curve* will be needed to demonstrate the presence of diabetes

4 *Blood studies*

(a) Blood count may reveal polycythemia
(b) There is no characteristic alteration of the electrolyte pattern

Diagnosis —The diagnosis depends upon finding the symptom complex described above, plus the confirmatory laboratory findings Arrhenoblastoma can be ruled out by pelvic examination plus the fact that while it masculinizes, it does not produce the metabolic changes seen in Cushing's syndrome Thymic tumors can be eliminated by chest x ray Pineal tumors and hyperostosis frontalis are easily eliminated

There are times when the diagnosis remains in doubt and a laparotomy must be done to determine the state of the adrenals However, this is

not to be undertaken until all other means of diagnosis have been exhausted, for Cushing's syndrome is rare and the suspected adrenals are usually normal Most fat, hairy women are, *horribile dictu*, simply fat, hairy women

CASE II *Benign Adenoma of Adrenal*—MISS F A, a white woman of 24 years, was admitted to the Episcopal Hospital on August 19, 1946, complaining of amenorrhea and purple spots on the skin She had been perfectly well until fourteen months before admission when her menses, which had always been regular, ceased abruptly At the same time she noted the appearance of purple spots on her skin For four months she had noted headaches, nervousness and pain in the low back This last had become so severe as to interfere with walking Two months before admission her ankles had become swollen A physician found her blood pressure to be "210"

The significant physical findings were the typical "moon face" and deposits of fat over the posterior neck and shoulders producing the "buffalo hump" appearance The skin appeared flushed, hirsutism was marked, and there were numerous purple striae over the abdomen The systolic blood pressure was 175 mm of mercury, the diastolic, 120 Examination of the optic fundi revealed a retinopathy of malignant hypertension Pelvic examination was negative There was pitting edema of the ankles and knee and ankle jerks were absent

Laboratory examination revealed a normal blood count, bleeding and coagulation time, prothrombin time and normal blood platelets Fasting blood sugar was 91 to 122 mg per 100 cc The glucose tolerance test showed a diabetic curve with the blood sugar at 268 mg per 100 cc at the end of three hours The Sulkowitch test was positive for increased excretion of calcium in the urine Serum protein was 5 9 gm per 100 cc and serum calcium 7 4 mg per 100 cc

X-ray of the skull in the lateral projection showed patchy demineralization The sella turcica was normal

X-ray of the spine showed generalized demineralization, and compression fractures of the first four lumbar vertebrae

The 17-ketosteroid excretion for twenty-four hours was 15 8 mg (increased) No gonadotropins were demonstrated and estrogen excretion was reduced

On December 3, 1946, Dr I M Boykin removed a 3 cm tumor from the left adrenal This proved to be a benign adenoma The patient had a stormy convalescence There were several episodes which suggested Addisonian crisis and which responded to adrenal cortical extract

X-ray two months after operation showed increased bone density in the spine suggesting recalcification

Follow-up examination six months later showed a remarkable change in the patient's appearance with recovery of the normal habitus and loss of obesity and hirsutism

COARCTATION OF THE AORTA

Coarctation of the aorta is a congenital stricture with partial or even complete obliteration of the aortic lumen There are two main types infantile and adult The infantile type is characterized by narrowing of the entire isthmus between the left subclavian artery and the ductus arteriosus Sometimes the narrowing is more extensive and there are associated serious anomalies [40] In the adult type, the narrowing is localized to an area at or just below the insertion of the ductus arteriosus

Patent ductus usually accompanies the infantile type, in the adult type it is usually closed

Since many of these strictures are now amenable to surgery, accurate and early diagnosis is important [14] When untreated, more than half of the sufferers die before the fortieth year of some complication attributable to the coarctation rupture of the aorta, bacterial aortitis, congestive heart failure or cerebrovascular accident

Clinical Findings —There are no characteristic symptoms Those most commonly seen are headache, dyspnea and vertigo [12] There are a number of physical signs

Hypertension The arteries of the upper extremities and neck frequently show forceful pulsation In marked contrast is the femoral pulse which is usually reduced or not palpable By simultaneous palpation of the pulses, the femoral pulse will be felt later than the radial [33] In the normal person, the blood pressure in the legs is higher than in the arms In coarctation there is usually a moderate elevation of the diastolic blood pressure in both the upper and lower extremities [46] There is marked elevation of the systolic pressure in the upper extremities, giving rise to a wide pulse pressure In the lower extremities, the systolic pressure is elevated little or not at all This difference in pressure between the upper and lower extremities is an important diagnostic criterion, more so than the actual levels of pressure The difference in pressure is of special importance in the diagnosis of those cases which have normal blood pressure in the arms

Evidence of collateral circulation is often present, usually in the scapular and interscapular regions The involved arteries become dilated and tortuous, and their pulsation can be seen or felt

Murmurs, one or several, may be heard in the chest There is usually a loud systolic murmur heard best at the base and often in the interscapular spaces This is probably caused by the coarctation itself Not infrequently there also occur murmurs due to the presence of a patent ductus or to the presence of valvular disease [40]

Hypertensive changes in the fundus are usually mild, and only a fourth of the patients show cardiac enlargement

Laboratory Findings.— X *ray of the chest* is a valuable aid in diagnosis [4]

1 Changes which are diagnostic

(a) Notching of the ribs This usually involves the posterior portion of ribs 4 to 9 It is due to erosion by tortuous, intercostal arteries and the notches may be single or multiple Their absence does not rule out coarctation Rarely, these lesions may be produced by other diseases, notably neurofibromatosis of the intercostal nerves and congenital arteriovenous fistulas

(b) Demonstration of the aortic stricture. At times this may be seen in the left postero anterior oblique film or it may be visualized following the injection of diodrast

2 Changes which are suggestive

(a) Absence of the aortic knob This is of most value in older patients since it may be absent in the normal young person.

(b) Left ventricular enlargement, widening of the ascending aorta or widening of the great vessels in the neck are all changes which may or may not be present

Other laboratory studies are of no aid in diagnosis

CASE III *Coarctation of the Aorta*—G G, a 12 year old white girl, was referred to Temple University Hospital on January 10, 1949, because of a murmur and anemia She had been sickly since infancy and had been hospitalized many times, twice for bronchopneumonia She had always been listless and inactive, had required more than the ordinary amount of sleep and failed to gain weight satisfactorily

Past medical history revealed nothing suggestive of rheumatic fever or its equivalents

The significant physical findings were as follows Blood pressure in the right arm was 150 mm of mercury systolic and 100 mm diastolic In the left arm the pressure was 140 mm systolic and 90 mm diastolic In the legs the pressure could not be obtained by the auscultatory method and no pulses were felt The heart was of normal size by percussion and the rhythm was regular There was a loud systolic precordial murmur heard best at the base

X-ray of the chest showed bilateral notching of the inferior rib margins and a small aortic knob

The other laboratory findings were normal

A diagnosis of coarctation of the aorta was made and on March 3, 1949, Dr J P Rosemond operated There was a localized stricture of the aorta just below the origin of the left subclavian artery and the ductus arteriosus was closed The stricture was resected and an end-to-end anastomosis of the aorta was done Recovery was uneventful

Examination of the operative specimen revealed a lumen about 1 mm in diameter The blood pressures, after operation, were right arm 115 mm of mercury systolic and 80 mm diastolic In the left arm it was 110 mm systolic and 70 mm diastolic In both legs it was 100 mm systolic and 70 mm diastolic

THYROTOXICOSIS

The classical features of hyperthyroidism are well known and usually the diagnosis is easily made Most physicians are aware that thyrotoxicosis causes a hypertension characterized by elevation of the systolic pressure and depression of the diastolic Difficulty in diagnosis arises when the classical features of the disease are absent With advancing age, the nervous manifestations of the disease decrease and, in fact, may be difficult to elicit The whole affair may be dominated by the cardiovascular complications Angina, auricular fibrillation or congestive failure may be the presenting problem and it is not a simple one For it is well known that thyrotoxicosis per se rarely, if ever, causes cardiac failure There is usually concomitant hypertensive, arteriosclerotic, rheumatic or luetic heart disease present [25, 34]

These atypical cases have been discussed under a variety of names "masked hyperthyroidism,"[8, 5] "apathetic thyroidism,"[31] "nonactivated type of hyperthyroidism"[30] and "hyperthyroidism masquerading as heart disease"[32] A correct diagnosis is of vital importance for they respond dramatically to surgery.

The patient is usually more than 45 years of age, looks older than the stated age and is apathetic rather than stimulated Eye signs are minimal or absent The thyroid is not significantly enlarged and its consistency may be normal, granular or nodular The heart rate is usually less than 120 beats per minute, a forceful apical impulse and bounding pulses are often absent The skin may be warm and moist or, in cases of long standing, cool, dry and wrinkled It often has a salmon hue The basal metabolic rate is usually less than plus 40 per cent and may be normal

Symptoms which are suggestive are unexplained weight loss or diarrhea, heat intolerance and transient bouts of unexplained auricular fibrillation The last, when due to thyrotoxicosis, is characteristically difficult to slow with digitalis

It is obvious from the foregoing that a final diagnosis must often be made by laboratory means Determinations of the protein-bound blood iodine and of the uptake of radioactive iodine are valuable aids but, for many physicians, are not available

A time tried and reliable test is a trial on iodine [37] A base line should be established by making daily determinations of the basal metabolic rate until the results are consistent The patient is then started on the usual therapeutic regimen with iodine If it is found that the basal metabolic rate decreases while the patient is taking iodine and rises when it is discontinued, this may be taken as proof of the presence of thyrotoxicosis

ARTERIOVENOUS FISTULA

Arteriovenous fistula is frequently listed as one of the causes of an altered blood pressure simulating essential hypertension Actually there should be no confusion if the blood pressure is carefully taken The systolic pressure may be elevated but the striking finding is a decrease in the diastolic pressure with a reduction in the mean arterial pressure

Arteriovenous aneurysm may be acquired or congenital The acquired type is commoner and follows a penetrating or nonpenetrating wound, usually the former The congenital type is often multiple and inaccessible to treatment

Clinical Manifestations [17, 41]—*Local*—The commonest sign is a continuous machinery murmur, with systolic accentuation, heard over the lesion A pulsating mass and increased warmth of the neighboring skin may be present There may be varicose veins around and distal to the fistula, with the edema, pigmentation and ulceration commonly seen in chronic venous insufficiency Immediately after the fistula is established, there may be signs of circulatory deficiency in the part, ranging from coldness to gangrene If the fistula is established before the epiphyses close, there may develop overgrowth of the part

General—The blood pressure is described above The effects on the heart depend on the size and duration of the fistula When it is large and of long standing there are tachycardia, cardiac enlargement and

ultimately cardiac failure. The cardiac output is much increased.[17, 41] Even severe congestive failure may be relieved by closure of the fistula [23]

Tests Which Aid in Diagnosis.—1 *Branham's sign* is slowing of the pulse rate and a rise in both the systolic and diastolic pressures when the fistula is closed by compression [7] This effect is abolished by atropine [27]

2 When veins proximal to the fistula are used, the venous pressure is higher and the circulation time faster than on the normal side [39]

3. Arteriography, when available, may reveal the site of the fistula [47]

4 Venous blood obtained near the fistula has an abnormally high oxygen content and this finding may be used in localizing the lesion [50]

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SYMPOSIA

1947

January (Chicago)	ADVANCES IN CLINICAL MEDICINE
March (Nationwide)	DIABETES
May (New York)	PEDIATRICS
July (Mayo Clinic)	BLOOD TRANSFUSIONS AND RH FACTOR
September (Boston)	SPECIFIC METHODS OF TREATMENT
November (Philadelphia)	DISEASES OF THE RESPIRATORY TRACT

1948

January (Chicago)	ENDOCRINOLOGY
March (Nationwide)	DISEASES OF DIGESTIVE SYSTEM
May (New York)	NEUROLOGY AND PSYCHIATRY
July (Mayo Clinic)	ANOMALIES OF THE HEART
September (Boston)	SPECIFIC METHODS OF TREATMENT
November (Philadelphia)	RECENT ADVANCES IN GYNECOLOGY AND OBSTETRICS

1949

January (Chicago)	DISEASES OF THE SKIN
March (Nationwide)	TREATMENT OF LONG TERM ILLNESS
May (New York)	CARDIOVASCULAR DISEASES ESPECIALLY HYPERTENSION
July (Mayo Clinic)	GASTROINTESTINAL CONDITIONS
September (Massachusetts General Hospital)	RECENT ADVANCES IN MEDICINE
November (Philadelphia)	1 MEDICAL EMERGENCIES 2 NUTRITIONAL DISEASES

*NOTE The volume year is given in italic type